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CHILDREN ARE NOT EXPENDABLE*

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BOSTON

IN A city such as Boston, which abounds in good homes and therefore good people and good children, it is disturbing to me, as judge of the Juvenile Court, to find a recent serious increase in delinquency. In fact, as of this date in the Boston Juvenile Court, we are over 100 cases beyond last year's total figure, with yet over three months to go. More disturbing is the fact that the crimes committed are serious offenses. Does this suggest that there has been a lowering of the standards of education, discipline and morality in youth?

It is not reassuring to find that in most cities through the country similar experiences are being recounted. In fact, the Federal Bureau of Investigation recently reported a rise in crime rates in the United States, and this increase was also described in the August 17 issue of the *New York Times* under the headline "Rising Crime Record a Grave City Problem." The following is a quotation from this article:

> There was shock and dismay last week when official New York police figures for the first six months of this year were made public. Figures show an increase over the first six months in 1951 in every category of major crime, ranging from 11 per cent to nearly 50 per cent.

The article further stated that the streets of New York were no longer safe and that New Yorkers today, in every walk of life, believe that there must be an understanding of the underlying cause for this rise in crime before effective steps can be taken to combat it.

Like most people who are closely associated with the education and care of children, I understand the underlying causes of crime. It is known, for example, that the juvenile delinquent of today is very often the criminal of tomorrow. Frankly, the chief causes of delinquency are recognized but cannot be removed. Most antisocial behavior could be stopped immediately if every child could be instantly provided with a well adjusted personality, with good companions and with conscientious parents in an economically and morally stable home, set in a pleasant suburban area containing maximum recreational facilities. Such a utopian set up would, indeed, remove the causes of most misbehavior.

* * *

I submit that the greatest cause of delinquency and crime is public apathy and ignorance, an apathy that allows the public not to insist on high standards of morality and service in every sphere of child life, as well as adult life, and an ignorance that does not recognize the long-range values of a well ordered life to the individual himself and to society as a whole; in short, an ignorance and an apathy that do not see that some citizens need facilities and help that are necessary to a well rounded, happy, adjusted life in the community.

How successful would the efforts of men and women of the medical profession — a profession with a history of sacrifice and service and high ethics — be in the understanding and treatment of illness and in stemming the tides of plague and epidemics if they and their predecessors had met with the same degree of public apathy and ignorance?

* * *

Medical history is full of the successful assaults on children's bodily diseases. After years of exhaustive research, the damage of whooping cough, scarlet fever, diphtheria and tuberculosis has been radically diminished through inoculation, vaccination, drugs, clinics and improved hospital care. Yet, in diseases like poliomyelitis and cancer, barriers must still be broken down and frontiers conquered. I have noticed that the efforts of physicians are successful mainly because they have been able to persuade the public to understand their program and to co-operate in the prevention of disease, the best way to control disease being to prevent it. By the same token, the best way to control crime and delinquency is to prevent it.

In juvenile-court work, advances in technics and therapies have likewise been made, especially for mentally defective children and for those who are emotionally disturbed. Psychometric testing, psychiatric and psychologic services, behavior clinics

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and enlightened institutional care have helped some children. But these means have not been developed to their true potential; in fact, there are not enough trained personnel or enough facilities for care or research. Some advances have been made, but in the social field the degree of progress attained in the medical field has not been matched. Much exploratory effort is still needed to find the right weapons to level the barriers encountered in work with many problem children.

As I have said, the primary factors are known, but because of apathy and ignorance there is not the kind of public support that would demand highly skilled, trained people and the essential facilities not only for studying and treating but also for anticipating and preventing the periodic increases in crime and delinquency. The public is not interested because most people believe that they are not directly concerned with the effects of crime or delinquency. Therefore, they do not co-operate with programs of prevention. This neglect is tragically shortsighted because there is just as great contagion in delinquency as there is in disease, to say nothing of the cost, which has been mentioned as amounting to over $11,000,000,000 a year.

Until two years ago in this state, which I consider one of the most progressive in the country, there was no temporary-detention study home to provide care at the time of arrest for children whom it seemed unwise to return to their own homes before their appearance in court, and a place that could also furnish the court, before disposition, with a study of the more disturbed children. Before the detention home on Huntington Avenue in Boston was opened children were held in police stations and lock-ups with vicious and hardened criminals. I am sorry to say that, though such a facility is now available for boys, there is none for girls, who must too often be held in police stations and jails. Again, up to three years ago, a sound classification system for children who had to be committed was lacking, and delinquents were sentenced to correctional institutions by age instead of by needs. There is still insufficient personnel or facilities for foster-home care and psychiatric, psychologic and even medical assistance to help solve the vexing problems of childhood and thus to prevent later careers of crime. Again, this is due to the apathy and ignorance of the public — it has been truly said that any community has only the crime and delinquency that it merits.

* * *

I recall a boy just eleven years of age who was a runaway from home, got into many difficulties, was in many courts and finally came before the Boston Juvenile Court. He was placed in a private school in a small town, where a general practitioner, in his medical examination, discovered symptoms of a tumor of the brain. The diagnosis proved correct, but it was too late. This boy should not have been considered a delinquent: his physical defect was only one of his handicaps. In remembering his neglect, I think of a little girl who was likewise considered merely a behavior problem, but whose parents did something about it. Her attitudes and conduct were rapidly wearing out the whole family. With the assistance of a skilled pediatrician, who noticed, I believe he said, the pigmentation of her eyes, she was thoroughly examined at the Children's Hospital, where it was discovered that she too had a tumor of the brain. Thereafter, her problem was understood, and she was placed under competent medical and psychiatric attention, away from her home; the parents were thus given an opportunity to care for the other children under normal circumstances, and the patient was prevented from unjustly being brought before the court at some later date. How much better it would have been if the boy's parents and community had also sought assistance to eliminate apparent delinquencies!

* * *

Despite specialization in medicine today, and despite the advent of penicillin, aureomycin and cortisone, it would be crass ignorance to scorn the value and the necessity of the old fashioned notions of rest, diet, sleep and serenity — the keystones of health and recovery from illness. Similarly, despite the excellent contributions of Dr. Arnold Gesell, of the Yale Clinic of Child Development, and of other reputable persons, some of the studies and recommendations of specialists handling problem children disapprove of the old fashioned notion that to build a sound child, and consequently a sound adult, the child must face salutary forms of denial and punishment, discipline and personal responsibility at an early age.

In most cases of delinquency, it is essential to realize that the rights and property of others and the good of society as a whole are considerations that universal experience has decreed to be of paramount importance. Consequently, the philosophy that sentimentally and automatically extenuates a delinquent's antisocial behavior because of unfortunate hereditary and personal and environmental handicaps blinds itself to reality. Reflecting sympathetically and dispassionately on the child's immaturity and vulnerability to wrong-doing, one can better serve his own and the general welfare by insisting that the delinquent understand his degree of accountability for his actions, and by endeavoring, at the same time, to ameliorate the conditions that fostered his misconduct.

* * *

I am sure that physicians will appreciate my deep concern over the extremes to which some theories of socialized justice may lead when I suggest that

they allow their minds to dwell momentarily on the implications of the term "socialized medicine."

I am reminded of a story of two farmers engaged in building a barn. They were working side by side on a scaffold, nailing boards. One of them observed that the other every once in a while threw away a nail; becoming curious he went down to the ground, examined the discarded nails, and found that they were perfectly all right.

"Zeke," he yelled up to his partner, "these nails are all right. Why are you throwing 'em away?"

"Pointed the wrong way when I took them out of my apron," replied Zeke.

"Don't be a fool," answered his friend. "Don't throw them away. Save 'em for the other side of the barn."

I realize, of course, that I may not have completely evaluated the numerous aspects of such a complex problem, but, like Zeke's friend, I hope to recover my points and work on the other side of the barn. I say this because I do not want it to appear that no progress has been made any more than I want it to appear that my remarks have exhausted all the alternatives to be considered in a discussion of the present-day crime problem.

* * *

I have often considered, metaphorically speaking, the juvenile court as a health department, social in nature. Just as doctors consider the physical health department as a necessary heart to the prevention and control of disease, I think of the juvenile court as the heart of the organizational programs to control and prevent delinquency and crime.

Only fifty years ago the first juvenile court was created in this country — in fact, I believe, in the world. It is interesting that the second such court was the Boston Juvenile Court, founded in 1906. The founding of these courts meant that within law, and according to law, special juridical agencies were created, as a result of the agitation and desire of people to take children out of the operation of criminal law. These courts were especially endowed first with the power and duty of protecting society in its rights of personal security, secondly, with obligation to help change the attitudes and conduct of juvenile offenders to conform to the dictates of accepted society and, finally, unlike the adult courts, at least in practice, they were charged to concern themselves with the prevention, and therefore the control, of delinquency and neglect of children by educational and protective measures within the community. The problems of the children and families referred to them are considered in secret and informal sessions, from which no stigma should attach to the individual or to the family. What has been learned about the problems of delinquency and neglect of children has not been available in any conceived and logical program because there has been no uniform research in the field of delinquency and crime.

In the Boston Juvenile Court there is a small research project. The cost of this project does not come out of public funds but is borne by agencies and individuals wise enough to see that to control crime and its forerunner — delinquency — there must be public education through sound preventive knowledge. I want to pay tribute to the members of the Rotary Club of Boston and to such charitable organizations as the Boston Junior Chamber of Commerce, Charles Hayden Foundation, Committee of the Permanent Charity Fund, Mason Fund, Moses Kimball Fund and Sarah A. Hyams Fund for their generosity and foresight in making possible the research project of the Boston Juvenile Court, which has already furnished vital information to the community, to the Legislature and to leaders in Boston and Massachusetts. The driving force in the founding of the Youth Service Board and the Detention Study Home was the Citizenship Training Group, the clinic of the Boston Juvenile Court. As a result of studies carried out by this research department, as far back as three years ago, the community was warned that, because of the depression, followed by a war and the threat of a new war, more neglect, delinquency and dependency among children could be expected.

It should be pointed out, however, that only a small part of this city, state and nation is being served. In many other jurisdictions, because of lack of research facilities, there was no clear picture of conditions, and therefore there could be no warning. There is no over-all accurate picture of the nature and extent of delinquency in this state, or in this nation, because of the lack of penetrating research and valid statistics.

If the analogy that the court is a social health department is correct, should the delinquent or neglected child be referred immediately to the court for necessary diagnosis and treatment rather than permitted to wait until the diseases of delinquency and neglect have become acute and therefore less curable? Unfortunately, the community considers the juvenile court as a place of last resort, rather than a place of hope and help. If parents and others waited until the acute stages of disease had ravaged their children before they referred them for treatment, clinics and hospitals would be places of despair and death, rather than refuges of life and hope.

In my field the reason given for considering the court the last resort is that people want to save the child from a record, even though the law prohibits the stigma of a record — a point in development experienced in medicine years ago in the reluctance of people to admit the presence of tuberculosis or insanity in members of their immediate families, who were therefore not referred for treatment until the acute and hopeless stages.

Research and education can make society recognize and enlist the help of the court, when neces-

sary, with socially maladjusted children. I do not mean by this that all children presenting a behavior problem should be immediately referred to the court. Rather, I am pointing out that when the delinquency, because of either frequency or gravity, could approach the acute and chronic stages, the child should be referred to the court; other preventive agencies such as hospitals, clinics, schools, recreational facilities and social agencies should be appealed to in cases in which delinquency might well be prevented.

When children are referred to the court, the court understands its functions through its probation officers and investigational technics, which include medical, psychiatric, religious and environmental adjustments. In short, it brings to bear, where and when needed, the necessary aids to achieving a happy adjustment of the child. Personal defects and complications and environmental obstacles must be understood and eradicated from the path of healthy and wholesome growth. The court in such a situation is the heart of the machinery, and should set in motion all the therapeutic and protective forces to help the child. The failure to refer children to the proper agency in time, together with the lack of facilities to meet the problems, again, are the result of public apathy and ignorance. To conclude this point, I should like to quote the words of Judge Harvey Humphrey Baker, the first judge of the Boston Juvenile Court, who said that the purpose of the juvenile court is "To put each child who comes before it in a normal relation to society as promptly and as permanently as possible, and that while punishment is not by any means to be dispensed with, it is to be made subsidiary and subordinate to that function." He continued: "While in most cases the public interest is best served by doing what is best for the individual, there are instances of offenses committed under such circumstances as to come to the attention of a large number of young people where an example may be more efficacious, and in such cases punishment pure and simple is summarily inflicted."

Stark realism dictates that the individual child, by training and discipline, be helped to shape his own character to attain sufficient maturity despite seemingly overwhelming obstacles. He must be helped to rise above demoralizing handicaps.

The help of the home, the school and the church, and other contributing forces that constitute the bulk of a child's environment, must be enlisted, and then one must work with him individually and realistically within the limits of these factors.

The family must assume the primary burden of responsibility for the delinquent behavior of children. Many parents, because of limited income, low intelligence, immoral make-up or warped social values, too frequently prove unequal to the task of rearing their children. The family is the basic unit of society, and when the family becomes undermined the whole nation suffers. The first consideration of any evaluation of the needs of children is their inherent necessity for a secure home life. They are instinctively dependent upon adults for protection. In a desirable home atmosphere they receive love and care, learning obedience to authority and to respect the rights of others. It is the spirit of loyalty engendered in a well ordered home that is translated in later life into service and successful citizenship. This loyalty is synonymous in a social sense with patriotism.

In considering the home one should give due regard to the recreation of children. The false philosophy that recreation could replace the home became prevalent during the war years, and it was recommended that children be responsible for their own recreation. This idea fostered an undesirable cleavage between play activities and adult supervision. It was forgotten how realistic youth can be. The children wanted not an imitation but a duplication of forms of adult recreation. The soda bar situated in an atmosphere patterned after night clubs, with juke boxes and dancing under soft lights, was one innovation that posed many severe problems. This pastime helped, among other things, to precipitate an increase in drinking by young people.

Projects that encourage separation between youth and adults during critical times can have reverberations in the health and moral standards of the young. Adequate adult supervision is still the sanest method of helping youth to learn what many people never comprehend — the difference between freedom and license.

In times of stress and strain children need more supervision and guidance, not less than they have always been accustomed to.

It is only partially true that teachers function *in loco parentis*. They cannot supplant parents and the home, and they should not be expected to carry the whole burden.

Although it cannot be denied that the schools are not expected to enthrall every child, it is fair to inquire if too much stress has been put on attempts to make school pleasant and attractive to children. It appears that the idea of school as a discipline is being abandoned, probably owing to the efforts of believers in so-called progressive education. The incidence of delinquencies in recent years — both urban and suburban and both court-adjudged and privately "adjusted" — indicates that it might be more salutary to subject all children to more rigid control and less "freedom," "self-expression" and "natural development." Undoubtedly, regardless of what approach is used to make schoolwork appealing to a child, there will still be many with "feet that creeping slow to school went storming out to playing."

Religious motivation should be a persuasive instrument in the lives of all. It has been said that

a lack of spirituality — a turning from God — is the underlying source of world chaos, and that only by a return to religious fundamentals and values can man survive. This is not naïve as some propagandists would have one believe.

A child without an active church affiliation is deprived of an additional safeguard, an extra oasis of contact and strength. Mere weekly church attendance is an efficacious discipline. Children buttressed by the strength and protection of religious principles will never fall prey to the specious ideals that have enmeshed the youth of other nations.

While helping children to inhibit socially rejected behavior, adults should check up on themselves. Parents may insist that youngsters be seen and not heard, but cannot stop them from listening and thinking — and imitating. Children copy the ideational patterns of those about them, and their own attitudes and conduct reflect the examples to which they have been exposed. Small wonder that a child is often bewildered by reactions to his behavior when he thought all along that he had been merely acting in conformity with what he had watched his parents and other supposedly responsible grown-ups say and do. Good example is still more potent than precept. It is quite understandable that many youngsters, subjected to the variable ethical practices of the present day, should find it difficult to learn the true norms of moral conduct.

It is the solemn obligation of those who direct the dissemination of information and entertainment to realize their responsibilities. The theater, the newspaper, the radio and now television are tremendously powerful forces in influencing the attitudes and actions of children. At times, these mediums are guilty of harmful inconsistencies. How can the youthful mind rationalize the procedure of certain publications that editorially thunder lusty jeremiads over a vicious sex crime and at the same time publish elsewhere questionable sketches and unwholesomely suggestive phrases that excite the lowest instincts?

It would be wise for parents to reindoctrinate themselves with the natural virtues of kindness, sincerity, tolerance and truth. Their children's social attitudes and conduct would be correspondingly benefited.

Children will always bear the mystifying trademarks that often defy one's best efforts to understand them and to rear them properly. Their lack of judgment, thoughtlessness, contrariness and selfishness are inherent traits in the growing-up process. Guiding them to successful maturity is the greatest challenge in life. In normal times the task is not easy; in times of crisis it is most difficult.

* * *

In conclusion, I think it is applicable to quote the charge that was given to the Boston Juvenile Court a few months ago on the occasion of its forty-fifth anniversary: —

Sustain those social forces that can find
True ways to aid weak youth's confused mind.
Advance, with all the vigor you command
And foster every forward-looking plan
That strives to ease the burdens of the young.
Remembering, ALL men His pardon seek,
Who said, when to Him little children trod:
"Forbid them not — for of such is the Kingdom of God."

ASYMPTOMATIC ISOLATED VALVULAR PULMONARY STENOSIS*

Diagnosis by Clinical Methods

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ISOLATED valvular pulmonary stenosis was until recently considered to be a rare congenital cardiac anomaly. Taussig,[1] in her text, states, "the author has not had the opportunity to study a proven case of pure pulmonary stenosis." Greene and his coworkers,[2] in 1949, reviewed the literature and found only 68 cases proved by autopsy in which both the auricular and ventricular septums were intact. It is now realized that this entity is not rare, as evidenced by the frequent communications that have recently appeared.[3-11] Many of the current papers[4-6,9] have emphasized the physiologic studies, particularly venous cardiac catheterization, in the diagnosis of this entity. Engle and Taussig[12] have stressed the severe form of the disease characterized by a patent foramen ovale, cyanosis and a greatly enlarged heart. Abrahams and Wood[8] have emphasized the recognition of the anomaly on strictly clinical grounds and have also pointed out the varieties of this condition, with the great differences between the mild and severe cases.

During the past eighteen months we have had the opportunity of studying 21 patients with this anomaly; 6 of this number were selected for the basis of the present report. A correct diagnosis was established in all cases by strictly clinical methods. The purpose of the present communication is to emphasize the facts that this potentially

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grave entity can masquerade as a mild and benign condition and that it can be diagnosed correctly in a high percentage of cases solely on clinical evaluation of the patient.

Case Reports

Case 1. L. R., a 14-year-old girl, had had no symptoms nor abnormalities in growth or development. A murmur was first noted at the age of 6 years during a routine pre-school examination. Physical examination at the age of 14 revealed a systolic thrill palpable in the 1st and 2d intercostal spaces. A systolic murmur was audible along the left sternal border, with maximum intensity in the 1st interspace. In this area the murmur was of Grade 5 intensity, was rough and grating in quality and extended throughout systole. The 2d heart sound in the 2d interspace was decreased in intensity and pure in quality. An electrocardiogram showed no abnormalities. On fluoroscopic examination the vascularity of the lung fields was normal, and the heart size was within normal limits. The main pulmonary-artery segment was prominent and demonstrated an increased amplitude of pulsations. The right and left pulmonary arteries were of normal size, but the pulsations were decreased in amplitude as compared with those in the main pulmonary artery.

Case 2. D. H., a 7-year-old boy, had had no abnormalities of growth or development. No symptoms were noted at any time. A murmur was first heard at the age of 6 years. A functional murmur was considered at that time, and the patient was referred to the clinic 1 year later. On physical examination a Grade 3 systolic murmur was heard along the left sternal border with maximum intensity in the 2d intercostal space. The murmur was rough in quality and ended in a 2d heart sound that was of normal intensity and pure. An electrocardiogram was within normal limits. Fluoroscopic examination revealed normal vascularity of the lung fields. The main pulmonary-artery segment was increased in prominence and showed pulsations of increased amplitude. The right pulmonary artery was of normal size. The pulsations were normal in amplitude and less than those in the main pulmonary artery. The heart size was within normal limits, and there was no suggestion of hypertrophy of either ventricle.

Case 3. C. P., an 8-year-old girl, complained of occasional episodes of spontaneous epistaxis since the age of 2 years, the only abnormality noted. At the age of 6 years a murmur was first detected. A diagnosis of a "septal defect" was made at that time. Physical examination revealed a systolic thrill palpable in the 1st and 2d intercostal spaces. A systolic murmur was audible over the entire precordium, with maximum intensity in the 1st interspace to the left of the sternum. The murmur was Grade 4 in intensity, rough and grating in quality, and holosystolic in duration. The 2d heart sound was pure, and decreased in intensity in the 1st interspace, and of normal intensity in the 2d interspace. An electrocardiogram revealed no abnormalities. Fluoroscopic examination showed a slight increase in the vascularity of the lung fields. The heart size was normal. The main pulmonary-artery segment was prominent, with an increased amplitude of pulsation. The right and left pulmonary arteries were of normal size. Their pulsations were normal in amplitude but less than the amplitude of the pulsations over the main pulmonary artery.

Case 4. S. N., a 5-year-old boy, had had a murmur since birth. No symptoms were present at any time. Physical examination revealed a systolic thrill along the left sternal border with maximum intensity in the 1st interspace. A rough, rasping, systolic murmur was audible over the entire precordium with maximum intensity in the 1st left interspace, where it was of Grade 5 intensity. The 2d heart sound was inaudible in the 1st interspace and faintly heard and pure in the 2d interspace. An electrocardiogram gave evidence of hypertrophy of the right ventricle. On fluoroscopic examination there was decreased vascularity of the peripheral lung fields. The main pulmonary segment was prominent and showed an increased amplitude of pulsation. The right and left pulmonary arteries were of normal size. The amplitude of the pulsations was considerably less than that of the main pulmonary artery. The heart was not enlarged, but the configuration indicated hypertrophy of the right ventricle. The auricular segment of the right cardiac border was prominent.

Case 5. J. G., a 14-year-old boy, had had no symptoms at any time. A murmur was first heard at 9 years of age and was thought to indicate a defect of the auricular or ventricular septum. Physical examination at the age of 14 years, when he was first seen in the clinic, revealed a patient who fell below the 10th percentile for both height and weight for his age. A systolic thrill was palpable along the left sternal border, with greatest intensity in the 2d left intercostal space. A systolic murmur was audible over the entire precordium, with maximum intensity in the 1st and 2d left intercostal spaces. In this area the murmur was Grade 6 in intensity, holosystolic in duration and harsh and grating in quality. The 2nd heart sound, which was inaudible in the 1st interspace, was faintly audible and pure in the 2d interspace. An electrocardiogram was within normal limits. Fluoroscopic examination revealed decreased vascularity of the lung fields. The main pulmonary artery was prominent and showed an increased amplitude of pulsations. The right and left pulmonary arteries were of normal size, with a decreased amplitude of pulsation. The heart was within normal limits in size, and the configuration suggested enlargement of the right auricle.

Case 6. D. M., a 5-year-old girl, had had a murmur since birth, and a diagnosis of defect of the ventricular septum had been made. No symptoms had been present at any time. On physical examination a thrill was palpable along the left sternal border with maximum intensity in the 2d interspace. A systolic murmur was audible over the entire precordium, with maximum intensity in the 1st and 2d left intercostal spaces. The 2d heart sound was faintly heard and pure in the 2d interspace and was not audible in the 1st interspace. An electrocardiogram revealed evidence of hypertrophy of the right ventricle and right auricle. On fluoroscopy the peripheral lung fields showed decreased vascularity. The main pulmonary artery was considerably increased in prominence and demonstrated an increased amplitude of pulsations. The right and left pulmonary arteries were small, and their pulsations were decreased in amplitude. There was enlargement of the cardiac silhouette, with a configuration indicating enlargement of the right ventricle and right auricle. Pulmonary valvotomy was performed on this patient in June, 1952.

Results

History

There was no limitation of activity in any of the cases presented above. On specific interrogation no symptoms suggestive of cardiovascular dysfunction were elicited. The parents would have considered these children normal in all respects if it had not been for their knowledge of a murmur.

Physical Examination

One patient (Case 5) was below average in height and weight; however, all patients appeared well nourished and well developed. The thorax was symmetrical in all patients. No cyanosis or clubbing was present. A presystolic pulsation in the neck veins was observed in 1 patient (Case 6). A systolic thrill was palpable along the left sternal border in 5 cases, being absent in 1 (Case 2). The thrill was of greatest intensity in the second left intercostal space in 2 patients, in the first interspace in 1, and of equal intensity in the first two interspaces in 2. On auscultation a harsh grating or rasping systolic murmur was audible over a wide area in every case. This murmur was of maximum inten-

sity in the first or second or in both the first and second left interspaces. The intensity of the murmur varied from Grade 3 in Case 2 to Grade 6 in Case 5. In every case the murmur definitely diminished in intensity on descending the left sternal border. Thus, in the cases in which the murmur was most intense in the second interspace, it was considerably louder in the first interspace than in the third interspace. In every case the murmur extended throughout systole. The second heart sound was decreased in intensity in the second left interspace in 4 of the 6 patients. In the first interspace the second heart sound was diminished or absent in all patients. The second heart sound in every patient was pure in quality.

Fluoroscopy

The lung fields were abnormally clear in 2 patients, and in the remaining 4 the vascularity was normal. The main pulmonary artery was increased in size in all. This prominence was slight in 3 patients, as shown in the chest film in Case 4 (Fig. 1). In the remaining patients the pulmonary artery was considerably increased in size. In another patient (Case 6) the enlarged main pulmonary artery was partially obscured by the enlargement of the right ventricle (Fig. 2). An increased amplitude of pulsations was noted in the main pulmonary artery in all cases. The right and left pulmonary arteries were of normal size in 5 patients and small in the remaining patient. The pulsations in the right and left pulmonary arteries were of normal amplitude in 2 cases and decreased in 4. All patients showed a disproportion between the increased amplitude of pulsations in the main pulmonary artery and the normal or decreased pulsations in the right and left pulmonary arteries. The heart size was within normal limits in 5 patients (Fig. 1) and increased in only 1 patient (Fig. 2 and 3). However, the configuration of the ventricular silhouette suggested hypertrophy of the right ventricle in 2 cases. There was prominence in the area of the right auricle in 3 patients, as shown in Figures 2 and 3.

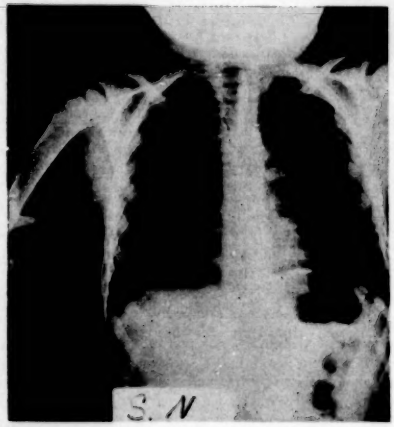

FIGURE 1. *Chest Film in Case 4, Showing a Cardiac Silhouette That Is Normal in Size, with Slight Prominence of the Main Pulmonary-Artery Segment.*

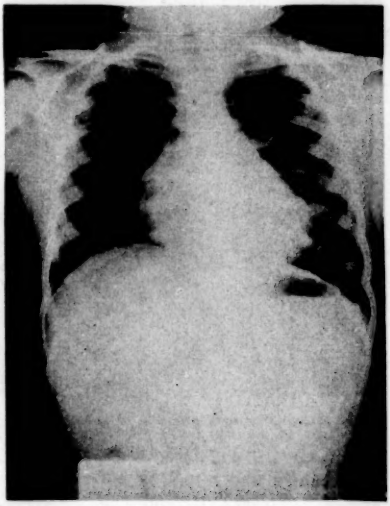

FIGURE 2. *Chest Film in Case 6, Showing Enlargement of the Right Ventricle, Which Partially Obscures the Enlarged Main Pulmonary-Artery Segment. The right auricle is also enlarged.*

Electrocardiogram

An analysis of the electrocardiograms is presented in Table 1. The electrocardiographic pattern was interpreted as falling within normal limits in 4 of the 6 patients. In 2, tall R waves, with a delayed intrinsicoid deflection time, were present in Lead V_1 and deep S waves in Lead V_6, indicating hypertrophy of the right ventricle. In 1 case there were tall, peaked P waves in Lead 2 and in the right-sided precordial leads (Fig. 4), suggesting enlargement or hypertrophy of the right auricle.

Physiologic Studies

Cardiac catheterization was performed in all 6 patients. Intracardiac pressures were recorded by the use of Statham strain gauges and a Hathaway recording apparatus. The point of 0 reference for measurement of intracardiac pressure was 10 cm. above the patient's back in the supine position. The as the tip of the catheter entered the right ventricle. The blood oxygen saturations gave no evidence of a shunt in either direction. The pressure within the right auricle was normal in 4 cases but definitely elevated in 2. The pressure tracings in these patients demonstrated characteristic large *a* waves as previously described by Abrahams and Wood.[8]

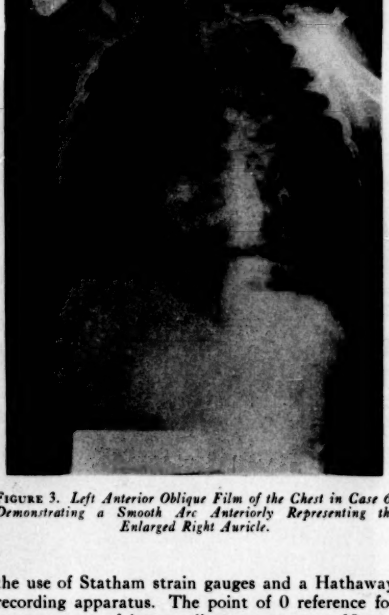

FIGURE 3. *Left Anterior Oblique Film of the Chest in Case 6, Demonstrating a Smooth Arc Anteriorly Representing the Enlarged Right Auricle.*

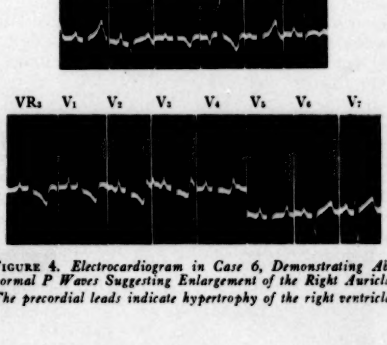

FIGURE 4. *Electrocardiogram in Case 6, Demonstrating Abnormal P Waves Suggesting Enlargement of the Right Auricle. The precordial leads indicate hypertrophy of the right ventricle.*

DISCUSSION

Although isolated pulmonary stenosis was until recently considered a rarity, recent reports have established the fact that this entity must be considered as a relatively common form of congenital heart disease. Also until recently there was a general opinion that patients with isolated pulmonary stenosis are markedly incapacitated, often cyanotic, and that fluoroscopy demonstrates a significant data derived thereby are presented in Table 2. The pressure tracing obtained on withdrawal of the catheter from the pulmonary artery into the right ventricle was diagnostic of pulmonary stenosis, showing an abrupt rise in systolic pressure decreased vascularity of the lung fields. It is now recognized that this lesion, like most pathologic entities, has a wide range of symptoms from the mild to the most severe, as emphasized by Abrahams and Wood[8] and Blount et al.[12] in the recent

TABLE 1. *Electrocardiographic Patterns.*

CASE NO.	ELECTRIC AXIS	QRS INTERVAL	INTRINSICOID DEFLECTION LEAD V1	AMPLITUDE OF P WAVE LEAD 2	AMPLITUDE OF P WAVE LEAD V1	RATIO OF AMPLITUDE OF R-WAVE TO S WAVE LEAD V1	RATIO OF AMPLITUDE OF R-WAVE TO S WAVE LEAD V6	INTERPRETATION OF TRACING
		second	*second*	*mm.*	*mm.*	*mm.*	*mm.*	
1	Normal	0.08	0.02	1.5	2.0	3:10	14:2	Within normal limits
2	Deviation to right	0.08	0.03	1.0	1.5	20:20	16:2	Within normal limits
3	Normal	0.08	0.02	1.5	2.0	8:5	14:2	Within normal limits
4	Deviation to right	0.08	0.04	2.0	2.0	16:6	5:7	Hypertrophy of right ventricle
5	Normal	0.07	0.02	1.0	1.0	8:11	14:0	Within normal limits
6	Deviation to right	0.09	0.05	3.5	4.0	35:0	7:8	Hypertrophy of right ventricle and right auricle

medical literature. The failure to appreciate the great difference between the mild and severe variants is still widespread. The present paper is intended to stress the clinical picture of the mild cases, and to emphasize its great difference from the more severe cases, when the clinical picture is more widely recognized.

Symptoms

There may be no symptoms whatsoever, as in the 6 cases reported above. All these children were active, and except for the presence of a murmur, the parents would have considered them entirely normal in all respects. The fact that such patients may have severe isolated pulmonary stenosis and yet show no symptoms of any description is not generally appreciated. This fact is well demonstrated in Case 6, in which the diagnosis of isolated pulmonary stenosis had not been considered prior to evaluation in this clinic. The apparently benign course had led to a diagnosis of Roger's disease. Physiologic studies, however, revealed that this child had severe pulmonary stenosis, with a systolic blood pressure of 183 mm. of mercury within the right ventricle. Thus, it may be seen that despite the apparently benign course, a definitely malignant process was in operation. Characteristically, these patients have minimal symptoms until toward the end of the natural history of the disease, at which time they deteriorate rapidly.

Physical Examination

The children in this study appeared normal in every respect; all were well nourished and well developed. None of them demonstrated the characteristic "moon" facies described by Abrahams and Wood.[8] There was no evidence of cyanosis in any of them. Large *a* waves were noted in the pulse of the jugular vein in 1 patient. The accentuation of the *a* wave was presystolic in time, as in the report of Abrahams and Wood.[8]

The cardiac impulse may be normal although in the patients with definite hypertrophy of the right ventricle a visible and palpable lift was detected in the third and fourth interspaces between the mid-clavicular line and sternal border. Pulsations were absent in the second interspace to the left of the sternum.

Several features noted on auscultation are considered to be of great importance in arousing suspicion of the presence of isolated pulmonary stenosis. A systolic thrill is usually present, and a loud, harsh, grating systolic murmur is almost always present. This murmur is of Grade 3 to 6 in intensity and is frequently of maximum intensity in the first instead of the second left interspace. In these cases, however, the intensity of the murmur is almost always greater in the first than in the third interspace. This is considered to be of great importance in the differentiation of pulmonary stenosis and a defect of the ventricular septum. The murmur is transmitted into the neck vessels although usually not as well as the murmur of similar quality of aortic or subaortic stenosis. It is not believed that there is any definite relation between the intensity of the murmur and the severity of the stenosis. A pulmonary diastolic murmur was not audible in any of the cases studied. There is confusion regarding the second heart sound at the base in isolated pulmonary stenosis. In all the cases presented above, the second heart sound in the second left interspace was of normal or decreased intensity, although the second sound was frequently inaudible. The second heart sound in our experience has invariably been pure in quality; however, other observers have described reduplication.

TABLE 2. *Results of Cardiac-Catheterization Studies.*

CASE NO.	INTRACARDIAC PRESSURE						PERIPHERAL ARTERIAL OXYGEN SATURATION	CARDIAC OUTPUT
	RIGHT AURICLE		RIGHT VENTRICLE		PULMONARY ARTERY			
	systolic	*diastolic*	*systolic*	*diastolic*	*systolic*	*diastolic*	%	*liters/min./sq. meter of body surface*
1	8	4	42	5	23	14	90.0	4.24
2	6	1	47	5	21	11	95.8	4.0
3	11	8	55	7	20	13	96.0	3.42
4	8	5	60	3	15	10	98.5	4.60
5	8	1	96	6	14	8	95.0	2.96
6	13	6	183	1	23	15	94.8	2.91

Electrocardiogram

The electrocardiogram may be of great value in establishing the diagnosis of isolated pulmonary stenosis. The electrocardiogram may be within normal limits in many cases, as in 4 of the patients discussed above. However, when it reveals hypertrophy of the right ventricle, it becomes a great aid in establishing the diagnosis. The other entities, such as defect of the ventricular septum and aortic or subaortic stenosis, that may be considered in the differential diagnosis would reveal a normal pattern or evidence of hypertrophy of the left ventricle.

The P waves are usually normal but, in the cases of marked hypertrophy of the right ventricle, may be of increased amplitude and sharply peaked in standard Lead 2 and in the right-sided precordial leads. Thus, an electrocardiogram revealing evidence of marked hypertrophy of the right ventricle in a noncyanotic patient with a normal exercise tolerance strongly suggests the diagnosis of isolated pulmonary stenosis.

Fluoroscopy

There are four important features that should be noted during the fluoroscopic examination of these patients: the post-stenotic dilatation of the main pulmonary artery, the vascularity of the lung fields, the size and pulsations of the main and right and left pulmonary arteries, and the configuration and size of the right chambers of the heart. The post-stenotic dilatation is present without exception in these cases. Invariably, the amplitude of the pulsations over the main pulmonary-artery segment is at the upper limits of normal or definitely increased. When the heart is considerably enlarged the post-stenotic dilatation becomes less apparent, being masked by the enlargement of the right ventricle, as demonstrated in Figure 3. The right and left pulmonary arteries may be entirely normal in size. The most important feature that deserves emphasis is the disproportion between the increased amplitude of pulsations over the main pulmonary-artery segment and the normal or decreased amplitude of pulsations over the right and left pulmonary arteries. This is usually a striking feature and immediately suggests the diagnosis of pulmonary stenosis. The over-all vascularity of the lung fields in these mild cases may be normal in all respects although the vascularity frequently appears somewhat diminished toward the periphery of the lung fields. The heart may be entirely normal in size and configuration; however, a normal-sized heart may show a configuration suggestive of hypertrophy of the right ventricle. The prominence of the right auricle in the presence of a normal-sized heart and in a patient with no evidence of failure of the right ventricle suggests the possibility of isolated pulmonary stenosis.

Physiologic Studies

Cardiac catheterization should be performed in all suspected cases. Caution should be employed, however, when the catheter enters the pulmonary artery, for rarely the diameter of the stenotic valve just accepts the catheter and the blood flow to the lung is completely obstructed. The child should be engaged in conversation at this time, and the operator alerted to withdraw the catheter if need should arise.

This procedure confirms the diagnosis and is of great value in determining the management of the patient. Clinical evaluation may well establish the diagnosis, but it fails to evaluate the severity of the stenosis. The systolic pressures within the right ventricle in these patients varied from 45 to 183 mm. of mercury. Although no one level can be established at this time as a dividing line, we believe as Brock[14] does that when the systolic pressure in the right ventricle is elevated to 75 mm. of mercury or above operation should be advised. Pressures of this level or higher suggest inevitable failure, and the operative risk increases as the heart enlarges. At lower pressure levels one might postpone operation without fear of rapid deterioration while the experience of the surgeon and the operative technic improve.

Differential Diagnosis

Several other congenital cardiac anomalies are frequently considered in patients with mild pulmonary stenosis. The diagnosis of isolated pulmonary stenosis was not considered in any of these patients prior to evaluation at this clinic. The anomalies most frequently considered were small defects of the ventricular or auricular septum.

There are several reasons for these errors in diagnosis. The first is failure to realize that patients with isolated pulmonary stenosis may have no symptoms whatsoever and no limitation of their exercise tolerance and also that in the mild cases there may be no evidence of hypertrophy of the right ventricle by either electrocardiographic or fluoroscopic examination. Secondly, it is not generally appreciated that with mild isolated pulmonary stenosis the vascularity of the lung fields may appear within normal limits. The third error is failure to evaluate the location of maximum intensity of the systolic murmur and the second heart sound to the left of the upper part of the sternum. A thrill is unusual in the patient with a defect of the auricular septum, whereas it is almost always present in the patient with isolated pulmonary stenosis. The vascularity of the lung fields is usually increased in patients with defects of the auricular septum, and there is no discrepancy between the amplitude of pulsations over the main and right and left pulmonary arteries. The second heart sound over the pulmonary area is usually widely reduplicated in the septal defect and frequently prominent; these findings are not observed in patients with isolated pulmonary stenosis.

The murmur of the *maladie de Roger* is rarely of maximum intensity in the first left interspace, whereas this finding is frequently present in patients with isolated pulmonary stenosis. The electrocardiogram is almost always within normal limits in the patient with *maladie de Roger*, and although it may be normal in the patient with isolated pulmonary stenosis it may suggest hypertrophy of the right ventricle. Finally, the general impression is that isolated valvular pulmonary stenosis is rare and that the *maladie de Roger* is common, whereas the contrary more closely approximates the true

status. Other entities that have been considered in patients with isolated pulmonary stenosis are idiopathic dilatation of the pulmonary artery and congenital aortic or subaortic stenosis. In the differentiation of subaortic and aortic stenosis from pulmonic stenosis, the quality of the murmur, the thrill and the qualities of the second heart sound may be of limited value owing to the similarity of these findings. However, the fluoroscopic and electrocardiographic findings should establish the correct diagnosis. Idiopathic dilatation of the main pulmonary artery may create some confusion on fluoroscopy, but such patients rarely have a systolic thrill and a harsh, grating systolic murmur. It is believed that clinical evaluation can result in the diagnosis of isolated pulmonary stenosis with a high degree of accuracy. The diagnosis was established on solely clinical evaluation in all the cases presented above.

Summary and Conclusions

Isolated pulmonary stenosis is not a rare congenital cardiac anomaly but one of the more common types.

Six cases of isolated pulmonary valvular stenosis are reported and discussed, with principal emphasis on clinical evaluation.

It is stressed that this entity exists in an apparently mild form, the patient appearing normal in all respects, and that the correct diagnosis may be established on clinical grounds with a high degree of accuracy.

Physical examination reveals a thrill and a harsh systolic murmur that is of maximum intensity in the first or second left intercostal space and is almost always louder in the first than in the third left intercostal space. The second heart sound in the first and second left intercostal spaces is usually decreased in intensity to absent, and though it may be of normal intensity, it is always pure.

The electrocardiogram may be normal or may show evidence of hypertrophy of the right ventricle of varying degree.

Fluoroscopic examination is of great importance in indicating the correct diagnosis. The poststenotic dilatation is always present, and a disproportion exists between the amplitude of the pulsation over the main pulmonary-artery segment and the right and left pulmonary arteries. The over-all vascularity of the lung fields may be within normal limits, although it is frequently slightly decreased toward the periphery. The heart may be within normal limits in size, or there may be evidence of hypertrophy of the right ventricle. The right auricle may be enlarged. Enlargement of the right auricle with a normal-sized heart in a patient without symptoms is considered to be a finding of significance and to suggest the diagnosis of isolated pulmonary stenosis.

Cardiac catheterization confirms the clinical diagnosis but is of greatest importance in determining the management of the patient.

Finally, it is again emphasized that the asymptomatic patient has a malignant process that, unless recognized early and corrected surgically, may be fatal.

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COMA IN INFECTIOUS MONONUCLEOSIS*

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THE systemic nature of infectious mononucleosis has been recognized for many years.[1, 2] The neurologic involvement of this disease has constituted a rare and important manifestation; less than 1 per cent of proved cases of infectious mononucleosis have shown central-nervous-system symptoms.[2] The clinical picture has been that of meningitis,[3-9] encephalitis,[10-13] meningoencephalitis,[14-19] encephaloneuronitis[20, 21] and neuronitis.[22-25]

As would be expected from these variable symptom complexes, the findings in the cerebrospinal fluid are neither consistent nor pathognomonic. However, abnormal findings usually noted are similar to those found in viral infections of the central nervous system — that is, clear fluid, moderate increase in pressure, a pleocytosis predominantly lymphocytic, normal chloride and sugar concentration, and increased protein.

In a recent review,[18] 85 per cent of the patients were reported to have recovered completely in periods ranging from a few days to several months.

Of the 37 patients with central-nervous-system involvement in infectious mononucleosis,[12, 18, 20] only 5 have been comatose. The pertinent data in the cases associated with coma so far reported are presented in Table 1. The rare association of coma with infectious mononucleosis, as well as the unique

TABLE 1. *Review of All Cases of Coma in Infectious Mononucleosis.*

CASE NO.	AGE	SEX	EVIDENCE OF INFECTIOUS MONONUCLEOSIS	NEUROLOGIC INVOLVEMENT	DURATION OF COMA	PERSONALITY CHANGES	CEREBROSPINAL-FLUID FINDINGS	REMARKS
1[13]	17 yr.	F	Generalized lymphadenopathy, splenomegaly, hepatomegaly and typical blood picture	Headache, nuchal rigidity, positive Kernig and Babinski signs, coma, convulsions, ataxia, opisthotonos, adiodochokinesis, nystagmus and paresis of 3d right cranial nerve	?	Irritability	Increased pressure; 100 cells per cu. mm., all lymphocytes; ++++ Pandy reaction.	No heterophil-antibody test performed; complete recovery in 55 days.
2[13]	15	F	Generalized lymphadenopathy, splenomegaly and typical blood picture	Headache, nuchal rigidity, ataxia, coma, convulsions and left hemiparesis	2 wk.	None noted	Increased pressure; 100 cells per cu. mm.	No heterophil-antibody test performed; complete recovery in 28 days.
3[13]	17	M	Cervical lymphadenopathy, pharyngitis, splenomegaly and atypical lymphocytes; heterophil-antibody test positive in dilution of 1:896.	Slurred speech, convulsions, coma, nystagmus, bilateral ankle clonus and left plantar extensor response	24 hr.	Irritability, forgetfulness and emotional lability	Normal pressure; 33 lymphocytes per cu. mm.; protein of 120 mg. per 100 cc.	Complete recovery in 14 days
4[13]	19	M	Axillary and inguinal lymphadenopathy; absolute lymphocytosis; heterophil-antibody test positive in dilution of 1:448.	Motor aphasia, disorientation; nuchal rigidity; bilateral Kernig sign; facial weakness; diminished pain and light-touch perception over 5th cranial nerve; coma.	24 hr.	Easy distractibility	Normal pressure; 120 lymphocytes per cu. mm.; protein of 136 mg. per 100 cc.	Complete recovery in 30 days
5[14]	16	M	Cervical lymphadenopathy; ulcerative and membranous pharyngitis; typical blood picture; positive heterophil-antibody test in dilution of 1:896.	Convulsions and coma	2 days	Not described	Clear fluid; 18 cells per cu. mm. (type not described).	Complete recovery; clinical picture complicated by serum sickness following administration of anti-meningococcic serum.
6*	49	M	Absolute lymphocytosis; heterophil-antibody test positive in dilution of 1:640.	Vertigo, nystagmus and coma	96 hr.	Apathy, irritability, depression and antagonistic attitude	Normal pressure; no cells; protein of 90 mg. per 100 cc.	No physical signs of infectious mononucleosis on physical examination; complete recovery in 16 wk.

*Case reported in text.

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clinical observations noted below, are considered to justify the following case report.

Case Report

A 49-year-old captain was well until 11:30 a.m. on September 11, 1951, when he experienced sudden nausea and vertigo while sitting in a classroom. There were no associated symptoms. The past history was not pertinent.

Physical examination revealed a moderately obese man who was rational, lying in bed quietly with eyes closed, and who resisted interrogation. There were no abnormalities in the skull. The cranial nerves were normal. A horizontal nystagmus was present, with rapid component to the left. The ears, nose and throat were normal. The neck was supple, with no adenopathy. The lung fields were clear. The blood pressure was 150/100. The heart sounds were distant, the rhythm regular, and the rate 90 per minute. There were no murmurs. The liver and spleen were not palpable, and no masses were present in the abdomen. There was no muscle weakness and no limitation of motion at the joints. The reflexes were normally active; none were pathologic.

Examination of the blood showed a white-cell count of 10,600, with 77 per cent neutrophils, 22 per cent lymphocytes and 1 per cent eosinophils, and a hemoglobin (Wintrobe method) of 13.8 gm. per 100 cc. The sedimentation rate was 21 mm. in 1 hour (corrected Wintrobe method). The nonprotein nitrogen was 28 mg. and the cholesterol 194 mg. per 100 cc. A blood serologic test for syphilis was negative. Urinalysis was normal, as were radiograms of the skull and chest.

The patient was placed on bed rest. On the 2d hospital day the nystagmus was less marked, but the vertigo persisted. A lumbar puncture revealed a cerebrospinal-fluid pressure equivalent to 160 mm. of water, with no cells, a total protein of 66 mg. per 100 cc. and a negative Wassermann reaction. The patient improved until the 7th hospital day, when coma supervened; a lumbar puncture at that time demonstrated a cerebrospinal-fluid pressure equivalent to 360 mm. of water, with no cells and normal sugar and chloride concentration. Daily neurologic examinations failed to show any abnormality other than the comatose state. The patient had a low-grade fever each day, the temperature not exceeding 100°F. by rectum. Continuous bladder drainage was necessary. Therapy consisted of prophylactic administration of penicillin, oxygen, parenteral injection of fluids and intermittent suction to maintain a free airway. The comatose state lasted for 4 days, after which the patient became alert enough to eat soft foods. He was transferred to the Zone of the Interior from overseas for further treatment.

On entry to the U. S. Army Hospital, Fort Belvoir, Virginia, the patient was lethargic, irritable and depressed, with suicidal behavior. His wife noted a change in personality since the onset of the illness; instead of a thoughtful, trusting person he had become irritable, thoughtless and suspicious. A lumbar puncture performed on the 30th hospital day showed a cerebrospinal-fluid pressure equivalent to 140 mm. of water, with 5 cells per cubic millimeter, a normal sugar and chloride concentration, a protein of 90 mg. per 100 cc., with a marked increase in globulin, a negative Wassermann reaction, and normal colloidal-gold curve. The white-cell and differential counts in both hospital admissions are summarized in Table 2.

Urinalyses were again normal. An oral glucose-tolerance test was negative, as were complement-fixation tests for lymphocytic choriomeningitis and mumps. A blood heterophil-antibody test on admission was positive in 1:640 titer. An electrocardiogram was normal. The icteric index was also normal. The thymol turbidity was 9 units per 100 cc.

The patient's appetite improved slowly. The vertigo was so prominent that he was unable to sit up in bed; this state persisted for 2 weeks after this admission before subsiding. The personality changes and vertigo gradually disappeared. Subsequent heterophil-antibody titers were 1:640, 1:160 and 1:320.

Discussion

Coma presents a perplexing diagnostic problem. An analysis of the 5 cases of coma and infectious mononucleosis previously reported and of the case presented above reveals several clinical variations, as well as suggestive diagnostic and prognostic criteria. It is clearly understood that the series presented is not significant statistically, but it is the largest series available on this topic.

Five patients were under the age of twenty years, 1 patient being forty-nine. There appears to be no sex predilection. In 5 cases physical examination gave evidence of infectious mononucleosis — that is, lymphadenopathy, splenomegaly or hepatomegaly. Five patients had evidence of disseminated involvement of the nervous system. The patient described above, on the other hand, had a negative neurologic examination while in coma, and was the only one with prominent personality changes. The cerebrospinal-fluid pressure was elevated in 3 patients. The protein content was elevated in all cases in which it was determined; there was a pleocytosis, predominantly lymphocytic, in 5 cases. All showed a complete recovery within a hundred and twenty days, with an average of fifty days.

The case reported is of particular interest because it appears to present an "atypical" clinical pattern: this patient was forty-nine years of age, had marked personality changes, with no evidence of infectious mononucleosis on physical examination, and a negative neurologic examination during the four-day comatose state. The cerebrospinal-fluid findings are of interest also in that the albuminocytologic dissociation had not previously been reported in comatose patients with infectious mononucleosis; the few patients so far observed all demonstrated the Guillain-Barré syndrome, which was not present in the case reported above.

Table 2. *White-Cell and Differential Counts.*

Date	Total White-Cell Count	Differential				
		Neutrophils	Lymphocytes	Eosinophils	Monocytes	Basophils
	$\times 10^3$	%	%	%	%	%
Sept. 11	10.6	77	22	1	–	–
Oct. 8	7.2	49	46	2	1	1
Oct. 25	8.8	56	42	2	–	–
Oct. 30	8.4	59	40	1	–	–
Nov. 13	7.75	54	36	7	2	1

This diagnosis, therefore, must be considered, together with acute infectious neuronitis, poliomyelitis, neoplasms of the central nervous system and diabetic neuropathy, which usually show an albuminocytologic dissociation in the cerebrospinal fluid.

The atypical pattern thus presented by the patient described above serves to emphasize the necessity of considering the diagnosis of infectious mononucleosis in any comatose patient.

Summary

The syndrome of coma and infectious mononucleosis is reviewed, and the highlights of the clinical disease presented.

The sixth case of the syndrome is reported. It is hoped that the unusual features demonstrated by this patient further emphasize the importance of considering infectious mononucleosis in the differential diagnosis of coma.

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BRAIN ABSCESS*

Influence of the Antibiotics on Therapy and Mortality

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BOSTON

BRAIN abscesses have consistently taxed the judgment and technical skill of the medical profession. The diagnosis is often difficult, leading at times to an unfortunate delay in operative intervention. Before the advent of present-day antibacterial therapy, early operation performed for a nonencapsulated abscess led almost certainly to the death of the patient. Yet to wait hopefully for encapsulation and reduction in the virulence of the infecting organism meant running a grave risk that the patient would succumb either to rupture of the abscess into the cerebrospinal-fluid pathways or to the effects of increased intracranial pressure secondary to this septic, expanding, space-taking lesion.

Two five-year series of brain abscesses, taken from the records of the Massachusetts General Hospital, have been reviewed as a basis for this communication. In the first, from 1936 through 1940, there were 25 deaths out of a total of 31 patients. In the second series, from 1946 through 1950, there were 29 patients and 10 died (Fig. 1). We wish to analyze and contrast our experience with these two groups, believing that the data here presented indicate that a further reduction in mortality can be accomplished and that such a reduction will in large measure depend upon the efforts of physicians and surgeons who are working in other fields than neurology and neurosurgery.

That there were 31 cases in the first series and 29 in the second might imply that modern antibacterial therapy has not affected the rate of occurrence of this lesion. Indeed, Pennybacker,[1] at Oxford, estimates that there has been an actual increase in the number of patients with brain abscess admitted to this hospital. It is his contention that present-day antibiotic medication has reduced the immediate mortality from bacteremia, meningitis and subdural empyema and that more patients survive such acute illnesses only to have a brain abscess later. On the other

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hand, the experience of any one hospital is notoriously unreliable as a basis for estimating the prevalence of disease in the general population. It can be said, nevertheless, that brain abscesses will continue to be a relatively common as well as difficult problem.

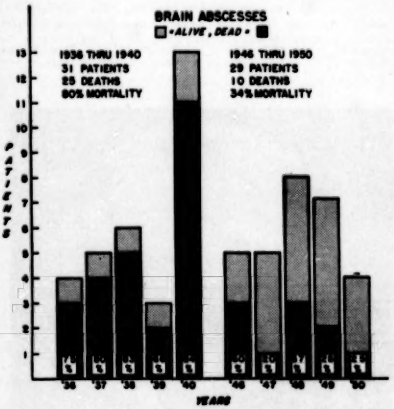

FIGURE 1. *Experience with Brain Abscess at the Massachusetts General Hospital from 1936 through 1940 and 1946 through 1950.*

MORTALITY RATES

Although statistics on the present-day incidence of brain abscesses may be somewhat equivocal, there has been an unquestionable change in etiology, which may be a factor in the improved mortality rate (Table 1).

From 1946 through 1950, no case of brain abscess was seen that was thought to be secondary to chronic sepsis in the lung or pleural space. In the earlier series, such cases made up 29 per cent of all brain abscesses, with a mortality rate of 90 per cent. More skillful surgical treatment of lung sepsis and bronchiectasis, in addition to improved bacterial therapy, has reduced the neurosurgical complications.

We should like to call attention to the deaths in both series that were secondary to head trauma. Once sepsis becomes established in a patient with a compound skull fracture, it may become a most difficult therapeutic problem. Yet experience with head wounds in World War II demonstrated that with proper débridement post-traumatic infection was rare. In all 4 of the cases referred to in Table 1 the wounds had been inadequately débrided before admission to the Massachusetts General Hospital. It is fair to say, particularly concerning the 2 patients in the second series, that these deaths should have been prevented.

It is obvious that the preoperative condition of the patient will significantly affect the mortality of any operative procedure (Table 2). We wish, however, to point out that the case mortality rate was formerly high even in patients whose condition was good prior to operation. All 4 of the deaths in this group followed drainage of a well formed septic focus. Death was due to inability to control the spread of sepsis consequent upon the surgical procedure. With a mortality as formidable as this, the surgeon was tempted to delay his operative attack, and as a result, from 1936 through 1940, 7 patients became comatose while being observed, and 5 of these 7 died. In the later series, while under neurosurgical observation 2 patients became comatose owing to rupture of an abscess into a ventricle. Fortunately, both patients survived this catastrophe by reason of prompt operation in addition to antibiotic therapy. In no case from 1946 through 1950 did death result from operative spread of infection at the time of aspiration or resection of the abscess. Furthermore, the advent of penicillin and other antibiotics encouraged the surgeon to operate early in the course of the patient's disease, and again in these latter years, no patient died from the effects of increased intracranial pressure who was not in profound coma prior to being seen by a neurosurgeon. In this connection, however, from 1946 through 1950, 9

TABLE 1. *Mortality Rate According to Origin of Brain Abscesses.*

ORIGIN	1936–1940 SERIES			1946–1950 SERIES		
	NO. OF CASES	DEATHS	MORTALITY RATE	NO. OF CASES	DEATHS	MORTALITY RATE
			%			%
Ear	6	4	67	13	4	30.0
Sinuses	7	5	70	3	0	0
Metastasis (lung)	10	9	90	0	0	0
Metastasis (miscellaneous)	1	1	100	7	4	57.0
Skull fracture	2	1	50	2	2	100.0%*
Post-craniotomy	1	1	100	1	0	0
Unknown	4	4	100	3	0	0
Totals	31	25		29	10	
Averages			80			34.5

*Both these patients were neglected and moribund on admission to the hospital.

patients were referred to a neurosurgeon after the onset of coma. Six of these died — a mortality rate of 66 per cent. Five of the 6 had well localized, encapsulated abscesses, and it can be assumed that

TABLE 2. *Deaths in Relation to Clinical Condition at Time of Operation.*

CONDITION OF PATIENT	1936–40 SERIES		1946–50 SERIES	
	NO. OF CASES	DEATHS	NO. OF CASES	DEATHS
Good	6	4	2	0
Fair	10	7	17	3
Poor	16	14	10	7

if earlier referral had been made, they would have had a good chance for recovery.

We believe, then, that complete débridement of compound fractures and early operation on patients who have not been allowed to become comatose offer the best opportunity for lowering mortality from brain abscess. Early operation, however, depends almost entirely on prompt recognition of the presence of a brain abscess through proper assessment of the patient. Here the problem has actually been complicated by the advent of antibiotic medication, which may allow expanding septic foci to develop in a much more insidious manner. Case 1 illustrates this problem.

CASE REPORTS

CASE 1. J. C. (M.G.H. 667943), a 15-year-old girl, entered the hospital on June 27, 1949, because of fever, headache and the sudden onset of a right hemiplegia. She had had a heart murmur since birth, and at the age of 6 years a mild cyanosis had developed. Her heart condition, diagnosed elsewhere as tetralogy of Fallot, was not so severe, however, as to limit her activities greatly. A diagnosis of subacute bacterial endocarditis with secondary emboli to the brain was made on admission, and although blood cultures were consistently negative, she was treated with large doses of penicillin. No lumbar puncture was done at that time.

It was noted that the patient's course was unusual in that she had convulsions limited to the right side of the body for several days at the beginning of her hospital stay. She also had persistent left-sided headache, nausea and vomiting and no return of function to the right arm or right leg. She was observed for 2 weeks and appeared to be in a stationary state. During the 3d week of her hospital stay, however, her condition began to deteriorate, with obvious drowsiness, increased headache, nausea and vomiting. On July 20 she became much more drowsy, with increased fever, and a lumbar puncture done at that time revealed a cloudy cerebrospinal fluid with 15,000 white blood cells per cubic millimeter, 95 per cent of which were polymorphonuclear leukocytes, and a spinal fluid pressure greater than 600 mm. of water. On the following day when the patient was barely responsive, one of us (H.T.B., Jr.) was asked to see her in consultation. A diagnosis of brain abscess was made, she was immediately taken to the operating room, and, through a small craniectomy opening just to the left of the mid-line over the coronal suture, a ventricular needle was introduced in the left parietal region, striking an abscess at a depth of 4 cm. A mixture of Thorotrast, penicillin and streptomycin was introduced into the abscess cavity, and x-ray films were taken (Fig. 2). The anteroposterior film suggested that the abscess had ruptured into the subarachnoid space rather than into the lateral ventricle.

The patient's state of consciousness improved somewhat after the tapping of the abscess, and she was immediately returned to the operating room for definitive attack upon the lesion. While a scalp flap was being turned down, however, she went into deep coma, and the anesthetist was unable to find evidence of cardiac or respiratory function. A rapid craniectomy was then carried out, and the abscess excised in toto. It ruptured during this procedure with gross contamination of the surrounding brain. The cavity that the abscess had occupied was thoroughly irrigated, and the wound was closed primarily with black-silk sutures. The patient was treated with large doses of penicillin and streptomycin, intramuscularly as well as intrathecally (Fig. 3). There was gradual improvement, and she was discharged from the hospital on

FIGURE 2. *Thorotrast-Filled Abscess Cavity As Seen in an Anteroposterior Roentgenogram (Case 1).*

August 26. At that time, she had a severe hemiparesis of the right side of the body that was worse in the right arm than in the right leg. There was also some degree of aphasia. In the year after operation the aphasia cleared completely. She still had some weakness of the right arm and leg but had been going to school and had appeared in school plays. In July, 1952, the bone defect left by the craniectomy was repaired with a tantalum plate.

This patient presented, in summary, the following salient findings: fever, headache and localized neurologic signs accompanied by seizures. A lumbar puncture earlier in the course of her illness would undoubtedly have disclosed a high cerebrospinal-fluid pressure and the presence of white blood cells,

indicating the need for earlier neurosurgical intervention. It should also be noted that brain abscess is frequently seen in patients with congenital heart disease. This case, previously unreported, represents one of the few survivals in this group.

Reference has been made to the fact that a brain abscess can now be operated upon at any time that evidence of increasing intracranial pressure or threatened rupture makes intervention imperative. It is not possible to standardize the approach to the therapy of these lesions, but, with individual variations, the following plan should offer the best chance for successful therapy.

Localization of the abscess. Often, the neurologic examination suffices for this purpose, as it did in the case described above. Occasionally, one must resort to ventriculography or arteriography. In either event, final localization must be made by the introduction of a ventricular needle into the septic area and the instillation of Thorotrast after the aspiration of pus. This is carried out through a trephine opening or a small craniotomy, which is subsequently closed. X-ray films are then taken to determine the exact position and extent of the septic focus.

Identification and specific treatment of the infecting organism. Immediately after the aspiration of pus and the instillation of Thorotrast, a mixture of 2 or 3 cc. of antibiotics of a wide range of potency (for example, penicillin and streptomycin or bacitracin and streptomycin) should be introduced into the abscess. A gram-strained smear of the pus is examined immediately under the microscope, and cultures are planted. If the condition of the patient permits it is wise to wait twenty-four to forty-eight hours for identification of the infecting organism and an opinion from the bacteriologist concerning the proper antibacterial agent to employ. For example, many gram-positive cocci that are resistant to penicillin have been shown by Meleney and his associates[2] to be highly sensitive to bacitracin.

Evacuation of the abscess. This can be accomplished by two methods, which may be used singly or in combination: repeated aspiration, and excision of the abscess. Whenever there is a threat to life from incipient rupture of the abscess into

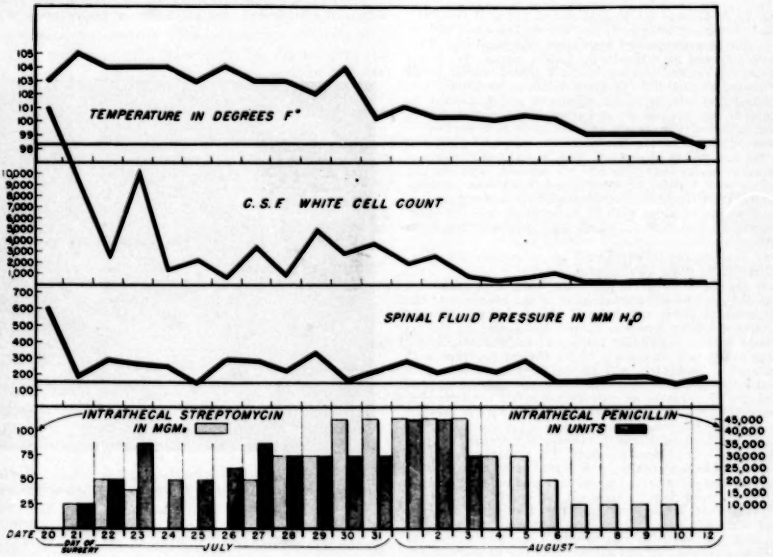

FIGURE 3. *Clinical Course and Intrathecal Medication Postoperatively in a Patient with Congenital Heart Disease and Brain Abscess (Case I).*

a ventricle or the effects of increased intracranial pressure, excision is the treatment of choice as in the case reported above.

When the clinical state of the patient permits and the abscess is located in an area of the brain vital to motor function, speech or vision, repeated aspirations should be given a trial. This method is well illustrated by the course in Case 2. It must be pointed out that this case, in which the patient was recently admitted to the hospital, was not included in the preceding tables, but is reported in some detail because of its teaching value.

CASE 2. A 47-year-old Englishwoman (M.G.H. 776754), who had previously been well, had the sudden onset of left-sided headache accompanied by nausea and vomiting. This was soon followed by difficulty in finding words. With this complaint she entered another hospital, where lumbar puncture revealed a spinal-fluid pressure within normal limits but 420 white blood cells per cubic millimeter and a spinal fluid protein of 56 mg. per 100 cc. Her symptoms persisted, and in addition to difficulty in speech, an inability to write developed. She was admitted to the Massachusetts General Hospital, under the care of one of us (J. C. W.), 2 weeks after onset of her symptoms. At that time she was severely aphasic and showed as well a right homonymous hemianopsia. Repeat lumbar puncture showed a cerebrospinal-fluid pressure equivalent to 188 mm. of water with 92 white blood cells per cubic millimeter, 58 per cent of which were polymorphonuclear leukocytes.

X-ray examination revealed no sinus or mastoid infection, and chest films were also normal.

A left carotid arteriogram performed soon after admission showed distinct upward displacement of the branches of the middle cerebral artery on the left. After this procedure a small temporal bone flap was turned down, and an abscess was found with a ventricular needle; 25 cc. of foul-smelling pus was evacuated, and 2 cc. of Thorotrast together with 10,000 units of bacitracin and 25 mg. of streptomycin were injected into the region of the septic focus. At the time of aspiration of the abscess no resistance was felt with the ventricular needle, indicating that no abscess capsule was present. Cultures of the pus removed at operation grew a fusobacterium, which proved quite sensitive to topically injected streptomycin as well as to chloramphenicol. The patient was treated with chloramphenicol orally in a 2-gm. daily dosage, with frequent counts of the red and white blood cells. Within a few days, the mild right hemiparesis had nearly disappeared, the right homonymous hemianopsia had receded, and the aphasia was reduced to the occasional loss of a word. Six weeks after admission to this hospital, she was allowed to fly back to England. It was advised that she be re-examined on her arrival, and soon after she reached England she was admitted to a hospital. At that time she first raised purulent sputum, which was thought to come from a bronchiectatic area in the lung. It is believed that this lung sepsis was the source of the fusobacterium grown from the pus in the brain abscess. Neurologic examination and lumbar puncture gave no evidence of further activity of the abscess. If the size of this abscess had necessitated immediate intervention as a life-saving procedure, we should have had no hesitation in performing a radical excision of the area of cerebritis although this would probably have resulted in a much more severe neurologic deficit.

If repeated aspiration is necessary, and if evidence accumulates that the abscess is multilocular or its capsule so dense as to defy collapse by repeated aspiration, this method must give way to excision. The most reliable indications of such a situation are persistence of increased intracranial pressure and progression or lack of regression of neurologic signs. This problem is illustrated in the following case history.

CASE 3. A 17-year-old boy (M.G.H. 761919) entered the hospital because of severe left frontal headache, blurred vision and weakness of the right hand. Six months prior to admission, he had had an infected elbow, which had been drained. A month later he had a brief episode of difficulty in finding words. He was then relatively well for 4 months, but 4 weeks before admission he had a severe left frontal headache followed in 1 week by increase in severity and constancy of the head pain and nausea and vomiting. Blurring of vision and increasing weakness of the right hand then developed. A lumbar puncture in another hospital shortly before admission revealed a cerebrospinal-fluid pressure equivalent to 570 mm. of water, with 1000 white blood cells per cubic millimeter and a protein of 78 mg. per 100 cc. On examination, the patient was confused. There was a high degree of papilledema. A definite right hemiparesis was present and was worse in the arm. The temperature was 99.5°F. by mouth.

A left carotid arteriogram taken immediately after admission to the hospital showed an absence of blood vessels in the posterior half of the left side of the skull. A parietal bone flap was turned down, and a subcortical abscess with an unusually thick capsule found in the left posterior parietal region. Over 50 cc. of greenish-yellow pus containing gram-positive cocci was aspirated from this abscess. Thorotrast, bacitracin and streptomycin were then injected into the cavity. A trephine opening was made in the parietal bone at the optimal point for retapping the abscess, and the flap was then tightly closed. Cultures from the pus grew *Staphylococcus aureus* that was sensitive to all the standard antibiotics. Postoperative x-ray study showed a huge multiloculated abscess (Fig. 4).

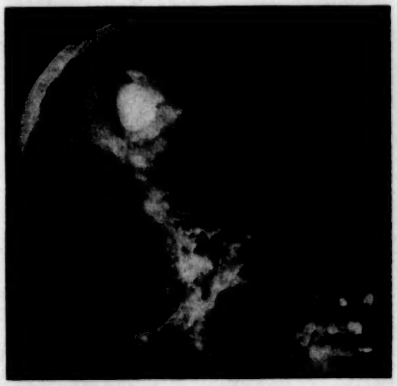

FIGURE 4. *A Large, Multiloculated Brain Abscess Partially Visualized by the Injection of Thorotrast into the Cavity—Lateral View.*

Despite daily aspirations and injections of 10,000 units of bacitracin and the intramuscular administration of large amounts of penicillin, the thick-walled cavity failed to collapse, and the patient continued to complain of headache and difficulty in speech. At the end of 1 week of this treatment he was vomiting and had become severely aphasic and hemiplegic. X-ray examination demonstrated no reduction in the size of the abscess. For this reason, the bone flap was removed, and the abscess exposed through a cortical incision just behind the parietal speech area. The capsule of the abscess, which was over 5 mm. thick in places, was opened, and its contents aspirated. It was then removed piecemeal without difficulty. The dura and scalp were then closed primarily, but a small rubber catheter was placed in the cavity

left by the abscess. Bacitracin and penicillin in 10,000-unit dosage were then injected via catheter and the lumbar subarachnoid space.

On the day after operation the patient was definitely less aphasic, and the strength in the right arm and right leg had improved. Within 1 week the right hemiplegia and aphasia had almost completely cleared. The dural clips marking the walls of the abscess had come together and for this reason the catheter was gradually withdrawn during the 2d week. He was discharged 16 days after resection of the abscess, when he showed only a very slight residual hemiparesis and aphasia with reduced position sense in the right arm and right leg.

Discussion

It is emphasized that one should not hesitate to excise an abscess when its presence constitutes an immediate threat to life. Excision might be thought to increase the chance of a neurologic deficit, and in this regard a recent report by Jooma et al.[3] indicates that resection of a temporal-lobe abscess is likely to be followed by lasting defects in the visual fields. Curiously enough, the same authors found that resection did not seem to increase the risk of a residual aphasia. In our later series, from 1946 through 1950, 8 patients had excision of dominant frontal-lobe or temporal-lobe abscesses. All 8 showed some degree of aphasia before operation that was increased postoperatively. In 4 of these cases, however, there is now no speech difficulty, and the others, although showing some degree of aphasia, are not so badly handicapped as to prevent their leading a useful life. One, for example, is in charge of student counseling at a large university.

Summary and Conclusions

The case mortality from brain abscesses has been reduced at the Massachusetts General Hospital from 80 per cent in the five-year period from 1936 through 1940 to 34 per cent from 1946 through 1950. The greatest single factor contributing to this reduction has been the advent of modern antibiotic therapy. With this aid there has not been a death traceable to operative spread of sepsis. Early operation has avoided, in many cases, the complications consequent upon rupture of the abscess into the cerebral ventricles or subarachnoid space. Death from the pathologic effects of increased intracranial pressure remains, however, all too common. Earlier referral to a neurosurgeon of the patient suspected of having a brain abscess should be most helpful in further reducing the mortality from this cause.

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MEDICAL PROGRESS

PSYCHOSURGERY

M. Greenblatt, M.D.,* and H. C. Solomon, M.D.†

BOSTON

In his presidential address before the American Neurological Association in 1941, Solomon[1] stated that the brilliant contributions to neurology since the time of Charcot had been based largely upon one methodology, which he called the jigsaw-puzzle technic. This depended upon observation of separate signs and symptoms, resulting from defects in the central nervous system, arranged in proper position until a complete picture emerged:

> If, however, we review the contributions thus made possible, it is seen that they deal very largely with the sensorimotor system. . . .The higher integrative functions of the brain. . . have been avoided . . . as not susceptible to study by the jigsaw trick. . . .When one looks at charts of brain localization, one is amazed that there have been no greater systematic attempts to meet the challenge of uncharted masses.

Since 1941, this challenge has been taken up with notable enthusiasm. In 1935 Moniz demonstrated that lobotomy could allay mental symptoms of psychotic patients, and in 1946 Freeman showed that it could relieve pain, opening up enormous possibilities for dissection of frontal-association areas and other zones in the human being. A rationale was provided for intensive reinvestigation of human brain function. It remains to be seen to what extent Solomon's prediction that "the established principles of neurologic study and reinvestigations will suffice to explore the functions of the brain other than those of a sensorimotor type" will be fulfilled.

This report is based primarily on studies of surgical treatment of mental disorder accumulated since 1948. Continuity with previous contributions may be obtained from other pertinent articles.[2-7]

Pathological Studies

Meyer and his co-workers have contributed perhaps the most significant studies in this field, owing particularly to the fact that their laboratory func-

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tions as a pathological clearing station for postlobotomy brain specimens in the British Isles. Part of their effort has been directed toward further elucidation of thalamic projection systems in man (McLardy,[8] 1950) and part toward study of the relation between location and extent of brain section and survival time, complications or degree of clinical improvement. We are concerned here with clinically relevant findings of pathological investigations.

The introduction of psychosurgery has had a definite and important effect on concepts of brain anatomy.[9] According to Meyer,[9] projections from the dorsomedial nucleus of the thalamus to the prefrontal cortex, from the anterior nuclear complex to the cingular cortex and from the anterior ventral complex to Brodmann's area 4 and 6 are highly organized. The anterior nucleus receives fibers from the hypothalamus via the mammillothalamic tract. There is at least oscillographic evidence that the projection from the dorsomedial nucleus also carries fibers from the hypothalamus to the frontal lobe. Most of the efferent projection systems of the frontal lobe seem to originate from its agranular parts. Direct tracts to the hypothalamus have been found in the neighborhood of area 6 and the posterior orbital cortex.

Comparative studies of primate and lower mammals reveal that development occurs not so much by acquisition of new areas as by increase in size of already existing regions. The only striking architectural difference within the frontal lobes is between the granular and agranular parts. Areal differences within the granular frontal region are relatively insignificant and variable. No rigid localization of specific mental faculties within self-contained regions of the granular frontal cortex would, therefore, be expected, from histologic evidence.

No significant clinical disturbances were noted by Meyer and McLardy[10, 11] in patients with bilateral cingulate lesions (area 24) or lesions in the claustrum, insula or uncinate fasciculus. Restlessness followed destruction of the posterior orbital area, prolonged incontinence followed both premotor and basal lesions, and early death from inertia, deficiency disease or trophic disorders followed posterior lesions. Two special forms of "delayed postoperative death" have been studied more intensively by McLardy[12] — namely, uremic death and death characterized by marasmus and trophic disturbances. According to McLardy, uremic death is likely to follow cortical damage of area 47, whereas bilateral damage to the subcallosal fasciculus leads to death characterized by marasmus and trophic disturbances. More specifically, connections between posterior area 47 and the head of the caudate nucleus must be cut to produce fatal uremia, and damage to the subcallosal fasciculus at the level of head of the caudate nucleus is necessary for trophic marasmic death.

In correlating type of brain section with improvement, Meyer and his co-workers[13] have reported that no specific coronal segment was always involved when improvement occurred, although section of the central segment came closest to being correlated with improvement. In general, the more segments involved and the more posterior the segments, the more likely the improvement. Personality changes were always marked in posterior cuts. There was some indication that orbital cuts yielded more satisfactory results than dorsal cuts, but the difference was not striking. Bilateral involvement of area 24 did not contribute to improvement but, in fact, tended to militate against it. It is of special interest that although the data as a whole point to better results in patients with relatively more damage, some remarkable cases of benefit followed minor cuts. One improved patient in Meyer's series had only a unilateral cut, and another a posterior incision with superficial bilateral damage to insular and opercular areas, but no evidence of damage to frontal association areas or thalamofrontal projections.

In 6 of their cases McLardy and Davies[14] reported that, despite almost complete bilateral isolation of the prefrontal cortex from its connections with long fibers, relapse occurred after improvement. The relapse must have been due either to return of pathologic activity via U-fiber systems, an unlikely possibility, or formation of new symptoms without prefrontal participation. This seems to support the concept that, although emotional tension is sustained primarily through activity of frontal circuits, the psychotic maladaptation involves the brain as a whole.

According to Meyer's work there is definitely a quantitative relation between degree of personality change and amount of prefrontal cortex sacrificed. Personality changes follow quite regularly upon bilateral lesions, and persist long after active repair and irritation have become quiescent, a consideration that prompted Meyer and McLardy to contradict the assertions of Hebb that there is no evidence of a frontal-lobe syndrome. Such a syndrome, indeed, exists, but there is no strong evidence for *localization* of function within the frontal lobes. Perhaps the orbital areas play a somewhat greater role in causing personality changes than other regions; for the most part, however, it is amount rather than location of cortex that determines personality change.[15, 16] Amount of cortex sacrificed in lobotomy must therefore be carefully assessed in relation to the patient's requirements.

Yakovlev and his co-workers[17] have contributed a careful neuroanatomic study of lobotomy emphasizing the marked parasurgical necrosis that occurs under most circumstances, especially when suction technics are used; and calling attention to the vast projection system of the frontal lobes, which are connected "in series" and "in parallel"

to all levels of the neuraxis. The illustrations in this study demonstrate beautifully degeneration in medial dorsal and anterior nuclei of the thalamus and massive demyelinization of fibers running from frontal areas to the pons.

Recently, Raskin et al.[18] have called attention to the apparent persistence of pathologic activity long after the original surgical trauma — if Gitter cells and macrophages may be considered evidence of continuing repair. Some of the patients surviving years after operation (1 survived more than five years) showed abundant microglial activity. This finding is consistent with the studies of Greenblatt and Atwell,[19] which demonstrated that the electroencephalogram is abnormal in a surprising percentage of patients followed for five years after frontal surgery, and psychometric performance suggests, for the majority of subjects, a deterioration in conceptual capacity.

Pneumoencephalography

Cortical atrophy in some schizophrenic cases has been shown pneumoencephalographically by Jacobi and Winkler,[20] Moore and Nathan[21] and Semrad and Finley.[22] Personality changes were greatest in schizophrenic patients with the most ventricular enlargement. Many neurosurgeons have noted, upon inspection of the brain at the lobotomy operation, thickened meninges and brain atrophy. Pool,[23] in particular, has remarked upon abnormalities occurring in fully 50 per cent of chronically ill mental patients. Although interpretations from gross observations of this sort are admittedly unreliable, the fact that similar reports have been received from many centers should not be neglected. Psychologic studies in chronic schizophrenia emphasize abstraction difficulties consistent with those found in known cases of brain damage.

Pneumoencephalograms before and after lobotomy have been done by Donovan et al.[24] and by Meschan and Scruggs.[25] They disclose not only preoperative abnormalities but also postoperative changes. The former workers found some degree of abnormality in all cases after operation, consisting essentially of enlargement of ventricles and widening of sulci. The most severe abnormalities were seen among older people with longer duration of illness. No clear correlation was noted between amount of atrophy and clinical outcome, although the authors suggest that major improvement tended to occur in cases with lesser degrees of postoperative atrophy. Meschan and Scruggs found progressive dilatation of all ventricles after operation, especially the anterior portion of the lateral ventricles, and progressive apparent obliteration of the subarachnoid space. Porencephalic cysts in frontal lobes were found in the postoperative pneumoencephalogram, as well as at post-mortem examination. These appeared to have formed most readily in cases with preoperative dilatation of the anterior horn, where greater possibility existed for entering the ventricle during operation. These findings suggested the need of preoperative pneumoencephalograms, especially when "blind" surgical procedures are used. In post-mortem examination of brain specimens the authors further emphasized atrophy and gliosis throughout the brain; meningeal thickening, scarring and hemorrhage; generalized enlargement of the ventricles; and cystic degeneration of thalamus and basal ganglions, especially the dorsomedial nucleus of the thalamus.

Physiologic Studies

Systematic and extensive studies of frontal lobes have been carried on recently at the Yale Laboratory of Physiology under Fulton.[26] These explorations in animals have been stimulated largely by the renewed interest in problems of the frontal lobes resulting from therapeutic use of lobotomy.

Stimulation of the primitive forebrain in the waking cat and squirrel monkey, of the olfactory tubercle and its associated stratum, the nuclei of the amygdala, the pyriform cortex and the portion of the hippocampus lying contiguous to the amygdala yielded attitudes of automatism seemingly related to eating or to the associated situations of fear, defense or attack that might beset the animal in the search for food and the struggle for existence. It is most interesting that stimulation of points close together sometimes resulted in completely different types of behavior; for example, in 1 experiment, stimulation of the region of the olfactory tubercle produced voracious eating, whereas, stimulation of a point 2 mm. distant in the amygdala resulted in dramatic spitting out and rejection of the same fruit. "The combined stimulation of the lateral nucleus of the amygdala and pyriform cortex resulted in arrest of the animal's movements in whatever posture he happened to be, the changing of the point of stimulation in the lateral nucleus to the rostral amygdala gave rise to directed attack or defense accompanied by hissing." (Experiments of McLean and Delgado.)

The increased appetite, overeating and weight gain of many patients after lobotomy, heretofore attributed largely to release of psychologic tension, may, however, be based on a physiologic mechanism elucidated by Delgado and Anend. Cats were stimulated for an hour each day by electrodes implanted in both sides of the lateral hypothalamus. A tremendous increase in food intake occurred, reaching 800 per cent of the original level. The effects were again due to very discrete areas, for movement of the electrode 2 or 3 mm. away from the effective point gave no change in intake of food.

Experiments in baboons by Pribram et al. comparing the medial frontal region with the lateral frontal region are of great interest to those interested in reducing the amount of brain damage of therapeutic lobotomy (while still maintaining the

beneficial clinical effects). Apparently, the lateral frontal cortex is involved chiefly in intellectual functions, whereas the medial subserves affective behavior. In another experiment, destruction of portions of the anteromedial or medial dorsal nuclei of the thalamus by the Horsley–Clark technic produced no deficit in performance of any of the delayed response-type tests. This suggests that frontal-lobe dysfunctions may not be primarily of thalamic origin.

In the *Macacus rhesus*, Rosvold and Brody demonstrated that frontal lobotomy serves to reduce fear in low-status monkeys, so that they frequently attack monkeys of higher status and thus rise in the social hierarchy. The direction of change was opposite to that in animals with temporal lobotomy in a similarly constituted social colony. These observations led to a prediction that in human beings, after frontal lobotomy, there would be less fear of aggressive and hostile behavior of others, that there would be defiance of authoritarian figures and a more aggressive handling of interpersonal relations. It is claimed that this prediction has been borne out by an analysis of family interaction during the process of rehabilitation of patients; however, it should be noted that another trend, opposite in direction and at least equal in intensity — that of decreased hostility, greater friendliness and sociability — has been observed through careful interaction analysis of patients before and after lobotomy by workers at the Boston Psychopathic Hospital.[27, 28]

Changes in human physiology following lobotomy have continued to be studied by a number of investigators. Peyton et al.[29] reported that there was no change in gastric motility and secretion after lobectomy. Reed[30] studied 9 cases of prefrontal lobotomy, all of which showed anacidity or subacidity prior to operation, but normal or increased acidity after operation. Carpenter[31] observed no effect of topectomy on gastric secretion — total acidity, free acid or combined hydrochloric acid — after five weeks. He stated that bilateral ablation of area 11, however, may inhibit secretion of hydrochloric acid. This issue continues to be clouded by positive and negative reports, partly because the brain lesions differ for different series of cases, and, partly, we suspect, because the personality changes also have their effect upon gastric functioning.

Donovan et al.[24] noted gain in weight in half their cases, but were unable to relate it to mental improvement. Buck and his associates[32] (in topectomy cases) were likewise unable to demonstrate a significant correlation of weight gain with either type of operation or response to treatment but noted a slight tendency to weight gain in the improved and to weight loss in the unimproved patients.

Thyroid function has been investigated by Brody and his colleagues.[33] No constant direction or degree of change occurred after operation in blood iodine concentration, cholesterol or protein, and no relation with postoperative clinical changes was apparent.

Buck and his co-workers[34] investigated temperature regulation of patients before and after lobotomy because their previous studies had shown that schizophrenic patients exhibited rigidity and irregularity in regulation of temperature compared to normal subjects. There was a definite tendency for the temperature cycle to revert to a more normal configuration after lobotomy. The more chronic schizophrenic group differed from the less chronic, in that the former were like the control patients preoperatively and changed very little postoperatively. "Chronicity" of mental disorder is conceived as being a burning out of the influence of the frontal lobes on autonomic centers; the same result is achieved more abruptly by prefrontal lobotomy.

Fall in blood pressure after lobotomy has been noted again (Donovan et al.[24]), the lowest level postoperatively occurred at the fourth to the fifth day. The fall was greatest if the blood pressure was originally high. Return to the preoperative level was the general tendency. Oltman and Friedman[35] studied the electrocardiogram extensively, noting a slight over-all decrease in tachycardia and a mild increase in incidence of premature beats. Ashby and Bassett[36] reported that patients with frontal-lobe operations showed individual peculiarities of physiologic responsiveness as compared to control psychotic patients who were not operated on.

Germane to the problem of frontal-lobe physiology in schizophrenia are the careful microchemical studies of Pope et al.[37] from the McLean laboratories. Taking advantage of the lobotomy trephine to obtain biopsies of frontal cortex, Pope has compared schizophrenic subjects with a "control" group of patients operated on for chronic psychoneurotic conditions and intractable pain. The mean acetylcholine esterase activity in cortical slices was increased in schizophrenia as compared to nonpsychotic patients. The range of esterase activity was significantly higher among deteriorated subjects with chronic schizophrenia than among patients with psychoneurosis or pain. If the high esterase activity is related to higher rate of acetylcholine turnover, the suggestion may be made that in some schizophrenic subjects there has been a chronic increase in the rate of neuronal discharge. An increased activity of frontal circuits has been invoked as an important neurologic mechanism in schizophrenia.

Electroencephalography

Kershman and Vasquez,[38] in 1949 confirmed previous reports of Cohn,[39] Levin et al.[40] and others that standard lobotomy resulted in continual random slow waves at 1 to 3 per second from anterior frontal and temporal regions. These gradually

subsided in four to six months but, in some cases, persisted for a longer time. Levin and Greenblatt[41] had previously shown that persistence of abnormality, increase in abnormality, persistence of focal signs or increase in focal signs suggested development of a convulsive disorder.

After recovery from dysrhythmia, a well organized background alpha and beta activity was usually present, sometimes higher in voltage than before operation. Intact thalamofrontal fibers apparently are not necessary for maintenance of normal alpha rhythm; both alpha and beta waves may be recorded from relatively isolated frontal cortex, and there may be extensive permanent damage to the white matter with little or no electroencephalographic abnormality.

Levin et al.[42] noted that electroencephalographic disturbances were as extensive after the bimedial as after the standard bilateral operation. Unilateral operation produced both unilateral and bilateral slow waves; the bilateral procedure caused gradual localization to the operated side and a tendency to disappearance of the focus over many months. The incidence of clinical seizure disorders after bimedial was equal to that after the standard bilateral operation; unilateral lobotomy yielded about half the convulsive complications of the standard operation. Lin and Greenblatt[43] showed that typical Pentothal waves were more pronounced over the intact frontal lobe in a case of unilateral lobotomy than over the operated lobe. Not only were Pentothal spikes suppressed or reduced in the operated lobe, but also the K complex, evoked by auditory stimulation during sleep, was diminished. Both methods are recommended as aids in localization of brain damage. They suggest that the barbiturate effect and the K-complex responses are dependent upon intact thalamocortical fibers.

Transorbital lobotomy has been studied by Henry.[44, 45] His 3 cases did not develop slow waves after operation; one of these patients showed a marked but transient increase in alpha activity from all head regions. (Two patients were operated on under electric-shock anesthesia, and the other under Pentothal.) There was no impairment in the amount, frequency or distribution of spindles during sleep, a finding contrary to that of Lennox and Coolidge,[46] who reported (in patients treated by standard lobotomy) the disappearance of 12-per-second spindles in frontal leads after operation, but no change in spindles of 14 to 15 per second.

The cortical undercutting operation has also been studied electroencephalographically by Henry. After undercutting, 10 of 11 patients showed alpha activity posteriorly that was as good as or better than that before operation. In 1 case a strong beat of 7 or 8 per second developed frontally, along with disturbed behavior; another demonstrated a sharp wave focus, together with clinical seizures.

Studies of Kristiansen and Courtois[47] in animals serve to establish on a firm footing the electroencephalographic observations on human patients after lobotomy — that the alpha rhythm is an inherent property of the cortex itself, not necessarily dependent upon thalamocortical circuits, and intensified in some cases by isolation of cortex from thalamic connections.

Liberson[48] has investigated the relation between postoperative electroencephalographic abnormalities and reaction time on word-association tests. Twelve patients with no electroencephalographic changes at three or four weeks after operation gave an average reaction time of 5.0 seconds for neutral words and 7.5 seconds for emotional words. A second group of 5 cases with considerable postoperative unilateral delta activity gave an average reaction time of 15.9 seconds for neutral words and 13.2 seconds for emotional words. Liberson believes that intelligence is affected to a much greater degree in patients with postoperative electroencephalographic abnormalities.

Results of Psychologic Tests

Intelligence

Elaborate tests of "biologic intelligence," which Halstead[49] devised for aspects of mental activity definitely related to brain function, failed to show impairment after lobotomy. Grassi,[50] in 32 cases, found no reduction in intelligence as measured by the Wechsler–Bellevue intelligence scale; there was, in fact, increased intellectual efficiency in 28 of 32 cases. Orchinik et al.,[51] in thalamotomy material, also observed no change in intellectual functioning by standard tests.

Against these findings is the report by Rylander[52] of definite loss in intelligence quotient; Rosvold and Mishkin[53] found intellectual impairment, especially if the preoperative psychotic level of intelligence was compared with the postoperative score on complex functions, and Petrie[54, 55] observed intellectual loss especially in tests tasking verbal ability and social comprehension.

Planning

This aspect of mental functioning is presumptively measured by the Porteus maze test. A drop of one and a half years or more in performance on the test, with subsequent recovery, has been reported after bilateral standard lobotomy.[56, 57] Landis and Ehrlick,[58] in a thirteen-month follow-up study of topectomies, reported transient loss in maze performance. The errors were essentially overshooting, nonperception, confusion and stereotypy. Patients who recovered tended to make more confusion errors after than before operation; this increased in the immediate postoperative period, and as clinical improvement occurred, errors were fewer.

Petrie,[54, 55] too, found a significant drop in maze performance. Porteus[59] himself tested maze performance after venous ligation, transorbital leukotomy, thermocoagulation and thalamotomy and observed a decline after all these forms of surgery. Porteus believes that planning is one of the chief functions of the frontal lobes and that recovery of planning capacity after operation suggests that posterior areas may, in part at least, assume this function.

A contrary note to the consistent trend discussed above was sounded by Fernandes,[60] who claimed an improvement in planning, foresight and initiative after psychosurgery.

Abstraction Capacity

Ackerly[61] stated that lobotomy patients could concentrate on only one thing at a time. Goldstein[62] believes that frontal lobotomy interferes with abstraction capacity just as frontal injuries interfered with abstraction capacity in his patients wounded in the war. Freudenberg and Robertson,[63] studying 24 patients (compared with 24 controls) before and six to eight weeks after operation, found that lobotomy produced significant loss in Koh's blocks performance, Bender gestalt test and paired-associates test. Grassi[50] noted organic changes in many of his cases as revealed in the graphic Rorschach test, and in the Grassi blocks test, but with a tendency to recovery during the first postoperative year. Petrie[54, 55] stated that capacity for generalization was definitely lowered after operation. Rylander,[52] too, reported that abstraction, as measured by proverbs test and fables and sorting tests, was poorer postoperatively.

In thalamotomy material, however, Orchinik[51] found no evidence of organic postoperative change.

Memory

Babcock[64] reported memory span to be shorter after operation. Rylander, however, found memory impaired only immediately after operation, and not after a lapse of a couple of months.

Creativity

Ashby and Bassett[65] studied creative ability in 25 cases and concluded that the operation did not lower scores for creativity that they devised. (This is the only systematic attempt to measure creative ability, and more such efforts are needed.) They tested the ability of a patient to add imaginative detail to a painting. Reitman[66] recorded 2 patients who underwent a creative spell after leukotomy that, however, soon subsided; Vencovsky and David[67] reported the appearance of creative artistry in 3 cases after operation. Freeman[4] mentioned several cases in which constructive intellectual work was performed after lobotomy; however, he also stated that creative ability is not consistently shown by anyone who has lost both frontal poles.

Hutton and Bassett[68] studied creative ability in 1 patient for nine weeks after operation. They noted on the Rorschach test decreased effort and application, lack of enthusiasm, quick, brief and conventional answers and generally reduced creative imagination.

Other Observations

Robinson et al.[69] have stressed lack of awareness of *self continuity* after operation, as well as reduced *sensitivity*. These changes were a function of the extent of frontal-lobe surgery. Wittenborn and Mettler[70] found that the patients' reactions after operation were determined more by immediate stimuli. Malmo and Shagass[71] reported greater responsiveness to external stimuli. In a setting of lowered muscle tension and steadier heart rate, outside stimuli appeared to have greater potency as shown objectively by withdrawal of the head from heat stimuli and by galvanic skin responses. In agreement with this experience is Penfield's[72] statement that patients subjected to gyrectomy show inability to maintain a set in the face of interference — suggesting greater distractibility by external stimuli. Petrie[54, 55] found less neuroticism and less introversion after operation. Some authors have noted greater ability to respond in social situations and greater productivity in work,[51, 52, 73] although quality of production often falls off.

Indications and Prognostic Criteria

In general, frontal-lobe surgery continues to be recommended primarily in cases with very poor prognosis. Judging from published reports, there has been no radical use of this procedure, such as to justify the alarm expressed during the early years of psychosurgery.

Arnot and his associates[74] carefully worked out prognostic criteria for identifying data, diagnostic entity, symptom picture and behavioral traits. As stated in that report, the best results were obtained in the psychoneurotic disorders (incapacitating obsessive-compulsive neurosis or hypochondriasis) and in the affective psychoses (involutional and manic-depressive psychosis). The next best results were reported in the paranoid psychoses (without hallucinations), dementia praecox, other types, and dementia praecox, catatonic type. Least benefited were the chronic manic conditions and dementia praecox, hebephrenic type. There is now general agreement on all these points.

Stevenson and Geoghegan[75] recently added their conviction that satisfactory results may be achieved in severe recurrent manic-depressive cases that have failed to respond to all other modes of management.

Worthing et al.[76, 77] and others believe that chronic hallucinations are an unfavorable sign.

The prognostic importance of "emotional tension," whether from anxiety, agitation, worry or self-concern, has repeatedly been confirmed. It is also generally agreed that excited impulsive behavior is usually greatly calmed by psychosurgery. Mackay[78] recently reported that violent outbursts were greatly ameliorated or placated in his series of 20 cases, including many patients with damage to the brain. Some reduction in behavior-disorder symptoms in children has been claimed,[79] as well as relief of epileptic furors and bursts of paranoid aggression.

Consideration has been given to the problem of the relation between alcoholism and lobotomy by Talbot, Bellis and Greenblatt.[80] Preoperative and postoperative drinking habits of 179 patients living in the community were evaluated. The great majority (93 per cent) did not change their drinking habits. Although 5 of 167 nonalcoholics became alcoholics for the first time after lobotomy, and 4 of 12 alcoholics drank more, 3 out of the 12 alcoholics stopped drinking entirely after lobotomy. It is clear that changes go in both directions, that the risk of alcoholism is in itself prohibitive of lobotomy and that prediction of direction of change is difficult.

Youth, a well balanced prepsychotic personality and acute onset of psychosis generally favor a good response to lobotomy. This has been reaffirmed by Johnson and Benjamin,[73] Moore et al.,[81] Fernandes and his co-workers,[60, 82] Heath and Pool,[83] Beller and Halpern[84] and Worthing and his associates.[76] That patients with shorter duration of illness often do better than those with longer duration of illness has been emphasized by Johnson and Benjamin,[73] Moore et al.,[81] Carscallen, Buck and Hobbs,[85] and Friedman and his associates.[86]

Koskoff and Weinger[87] and Tucker and Dynes[88] call attention to the necessity for viewing the family constellation psychodynamically before a lobotomy is undertaken. Whereas in psychotherapy the changes are slow, in lobectomy, they are fast, and the family may become upset by the "disinhibition" displayed in the postoperative period. One of the major problems is adjustment of the family to improvement that is partial and leaves a dependent, often handicapped person, who may not be able to contribute to his own support because of failure in a competitive labor market.

Patients who show a tendency to remission during the course of illness often respond well to lobotomy; the tendency is evidently a manifestation of recovery potential. This potential may be brought forth with somatic therapy. Kalinowsky and Scarff[89] and Worthing et al.[76] use the electric-shock response as a prognostic sign, although Carscallen, Buck and Hobbs[85] have not witnessed any clear relation between the response to electric shock and prognosis with operation. Fernandes and his associates[82] believe that the response to both electric shock and insulin is helpful in prognosis. Attempts to formulate predictive indexes based on response to intravenous administration of Amytal have been made by Feld[90] and by Spatz and Funk.[91] The former author claimed that in 9 out of 10 cases, postoperative results resembled strikingly the condition observed in the postnarcotic period. The work of Spatz and Funk shows a trend in the same direction.

Of great interest are the experiments in which procaine has been injected into the frontal white matter for the purpose of producing temporary physiologic separation of frontal cortex from the rest of the brain. Putnam[92] administered procaine by the transorbital route in several cases and observed characteristic clinical features of interference with frontal white matter that lasted two days to two weeks. In 3 of 4 cases lobotomy was performed with similar, but lasting, effects. Bailey et al.[93] have experimented with the use of procaine in 22 cats. They found no untoward reaction unless the procaine entered the subarachnoid space or the ventricle, in which case an immediate fatality resulted. With improved technic, this complication was avoided, and in man, adhesions were created between the arachnoid and cortex prior to injection, to prevent escape of the anesthetic. Histologic evidence of damage from procaine was slight. Van Wagenen and Liu[94] tried procaine in a series of patients later subjected to lobotomy and reported that the technic was most useful in the prediction of relief from pain and in psychotic patients was most reliable during the period of overactivity. Prediction was considered satisfactory in 2 out of 3 cases.

The relation of body type to clinical outcome after topectomy has been studied by Kline and Tenney.[95] Using Sheldon's classification, they found a significantly better outcome for mesomorphs than for others.

Engler[96] has observed the effects of lobotomy in 44 mental defectives followed for one and a half to three years. Most of them were low-grade imbeciles and idiots, 16 having epilepsy in some form, and 15 having added psychosis. All were restless, excitable, unstable or destructive. The results were unsatisfactory, for 5 died during the first year, 4 had increased severity and frequency of pre-existing epileptic seizures and 3 experienced epileptic attacks for the first time. Behavior improved strikingly in 5 per cent and slightly in 18 per cent, but many patients became worse. Engler has decided to abandon the operation in this group of cases.

(To be concluded)

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MEDICAL INTELLIGENCE

CROSS-SENSITIVITY TO DIPHENYLHYDANTOIN SODIUM AND TO PHENOBARBITAL

Report of Two Cases

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BOSTON

THE phenyl-derived anticonvulsant drugs described by Putnam and Merritt[1] have been in use for over fifteen years. Although they have been found to be of great value in the control of epilepsy, both mild and serious side effects have occasionally followed their administration. Gingival hypertrophy, dermatoses, ataxia, bone-marrow depression, hepatitis, nephrosis, twitching of the muscles, lapses into gradual sleep or coma, pancytopenia and fatal aplastic anemia have resulted from the use of these drugs.[2-4]

Phenobarbital has been widely used for several years, and its administration has resulted in such side effects as skin eruptions, incapacitating drowsiness, headaches, apathy and ataxia.

Diphenylhydantoin sodium has been known to cause all the toxic reactions characteristic of the group. It may produce restlessness, nervousness, nausea, vomiting, gingival hypertrophy, ataxia, dermatitis and various psychotic symptoms.

Ruskin[5] called attention to cross-sensitization in a single patient to phenobarbital and Dilantin, and also to a sulfonamide, but emphasized chiefly a fulminating fatal dermatosis from Mesantoin.

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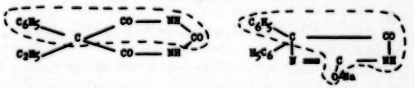
In this paper, we wish to emphasize the cross-sensitization of 2 patients to phenobarbital and diphenylhydantoin sodium, with recovery of both when the medication was stopped.

The chemical structures of phenobarbital and diphenylhydantoin sodium are as follows:



The similarity of the two structures is evidenced by a comparison of the portions enclosed by the dotted lines.

CASE REPORTS

CASE 1. A. J., a 60-year-old woman with epileptiform seizures, was seen at the Long Island Hospital suffering from a generalized vesicular and erythematous rash, which developed after 2 years of phenobarbital therapy in a dosage of 0.09 gm. (1½ gr.) twice daily. Vesicles, erythema and crusting with intense itching occurred on the back and on the sides of the arms and legs, as well as on the trunk. A diagnosis of dermatitis medicamentosa was made, and the phenobarbital was stopped; she was then given cold compresses and a dusting powder as local therapy. The eruption cleared over a period of 17 days, and the patient remained well for 21 more days. At that time, she was started on diphenylhydantoin sodium, and within 48 hours a vesicular erythematous eruption of the trunk similar to the one resulting from phenobarbital developed. The diphenylhydantoin sodium was stopped, and the rash again cleared, but the patient died of bronchopneumonia before either phenobarbital or diphenylhydantoin sodium could again be administered for diagnostic testing purposes.

CASE 2. Soon after this, Mrs. E. J. was seen in the office of one of us (G.E.M.) with an erythematous eruption of the face, chest, armpits and groin, which had developed after 1 month of diphenylhydantoin sodium therapy. A diagnosis of dermatitis medicamentosa from diphenylhydantoin sodium was made, and the drug was stopped. She was then given cool colloidal baths, antihistamine tablets and cold compresses, with complete recovery. After the eruption had been cleared for 6 weeks, the referring neurologist prescribed phenobarbital; within 24 hours the face and trunk became itchy, and an erythematous eruption developed. No more phenobarbital was administered, whereupon the rash cleared, and she has since been controlled on bromide therapy.

SUMMARY AND CONCLUSIONS

Minor and serious side effects may result from anticonvulsant drugs.

Diphenylhydantoin sodium has been reported to cause such side reactions as gingival hypertrophy and various types of dermatoses.

Two cases in which cutaneous eruptions followed ingestion of two closely related drugs — phenobarbital and diphenylhydantoin sodium — are reported.

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DOCTORS AFIELD

Charles Wendell Townsend

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CHARLES Wendell Townsend (1859–1934) was undoubtedly better known as an ornithologist and as a writer than as a physician. Until his retirement in 1917, however, he was "one of Boston's most skilled obstetricians and an authority on the nutrition of children."[1] He graduated from Harvard Medical School in 1885. He was said to have been a brilliant student, and in 1928 he was made an honorary member of Phi Beta Kappa.[1] He had a brisk practice in obstetrics (then apparently a medical specialty) and in pediatrics. He married in 1891 and in 1892 acquired a house in Ipswich, Massachusetts, where he made many of his observations of nature.

For about fifteen years after his graduation from medical school he tended strictly to his medical work. However, after 1902, his list of publications on the subject of birds and nature is impressive. His *Birds of Essex County*, published in 1905, is still considered pre-eminent in its field. Besides numerous articles in various ornithologic journals, he wrote a series of popular books, of which *Sand Dunes and Salt Marshes* is probably the best known. This is a "delightful account of the natural history of the dunes and marshes" (of Ipswich).[2] *Beach Grass*, which also deals with Ipswich, appeared shortly after, and was followed by several books about the Labrador coast, the result of repeated visits there between 1906 and 1915. His last book, *From Panama to Patagonia*, was published in 1931.

When I first became acquainted with Dr. Townsend, I was skeptical about some of his casual diagnoses of birds, but I soon learned to respect his great ability in field observation. Only once did I stump him.

"Dr. Townsend," said I. "Did you ever hear a crow sing?" And I went on to describe how on two occasions I had heard the sweet love notes of a crow. He looked at me incredulously. "No, I haven't," said he politely, and he never again alluded to the matter.

A friend wrote of him: ". . .and although fond of argument — in which he was quite sure he was always right — he was by nature considerate and kindly."[2] I well remember an argument at the Nuttall Club that took years to settle. At one of the meetings a young member rather casually asked if rabbits could sing. Dr. Townsend immediately pointed out that rabbits could thump, whistle and squeal but could not sing.

The president of the Club, the late Dr. Glover M. Allen, then somewhat facetiously remarked that there were reports from Australia of rabbits becoming carnivorous and starting to make singing noises (reports that later proved to be erroneous). President Allen suggested that perhaps the rabbits referred to had taken to eating young terns. But Dr. Townsend would not be put aside.

"What was the song like?" he wanted to know.

"Mm, mmmmmmmmm-mm, mmmmmmm-mm," said the young man.

"Why that's the song of the Leach's petrel!" exclaimed the doctor. (Leach's petrel had not then been known to nest west of the Maine Coast.)

The young man smiled. "We watched the hole for hours and finally a rabbit came out. So we decided it was the rabbit that was making the noise."

Dr. Townsend was not convinced. A committee to investigate the matter was appointed and, at the Club's expense, spent several days of the following July on Penikese Island. The report was the same. "Mm, mmmmmm-mm, mmmmmm-mm," from the hole. Rabbits came out, no singing; rabbits came back, singing.

"I don't care," said the Doctor, "that's the song of the Leach's petrel. I move that another committee be appointed and I ask to be made a member of it."

This was done. Rabbits came out, no singing; rabbits came back, singing. But this time, owing to the Doctor's persistence, the watchers waited. And sure enough! A short time before sunrise a pair of Leach's petrels came out of the same rabbit hole. Thus was established the record of the westernmost nesting site of this petrel, and once more Townsend's reputation for accurate observation (as well as obstinacy) was enhanced.

I saw him professionally two years before he died. X-ray films showed a carcinoma of the stomach. At operation, the growth was so extensive that its removal was out of the question. It was already causing pyloric obstruction. Posterior gastroenterostomy was technically impossible.

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"Everybody claims it's wrong," said the surgeon, "but I'm going to do an anterior gastroenterostomy," and he proceeded to go ahead with it.

Dr. Townsend recovered rapidly, regained his lost weight and strength, and not long after made a circuit of Africa by ship, with many land excursions thrown in. He lived in comfort for nearly two years. When at last the tumor caught up with him, he quickly began to fail and died in a few weeks. This extraordinary response was possibly due to his wiry strength, possibly to his surgeon's willingness to do the wrong thing and possibly to luck.

However that may be, while the descendants of his patients will probably never have heard of him, the "Sage of Ipswich" as he was sometimes affectionately called, will long be remembered as a competent naturalist and a fine ornithologist.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 39011

PRESENTATION OF CASE

A seventy-six-year-old woman was admitted to the hospital because of progressive weakness.

Ten years previously the patient noted the onset of slight exertional dyspnea and edema of the legs; the latter was usually worse in the evening and disappeared by morning. Both symptoms gradually became more marked, and were most troublesome during the year prior to entry. Digitalis was prescribed by her physician, and the symptoms improved although ankle edema tended to recur. Three years before admission progressive weakness developed. Despite these symptoms the patient was active, although limited to some extent by poor vision, until one month before admission, when, while out shopping, she suddenly felt "staggery," had trouble stepping over curbstones, and required help getting home and up one flight of stairs to her apartment. Although she had no recurrence of staggering or dizziness she dated her decline as beginning with this episode, after which she noted a marked increase of edema with involvement of the arms during the week before admission, diminution of vision in the right eye, progressive severe weakness, dyspnea and anorexia. Urinary frequency, said to have been pronounced for years, became more marked, but she denied thirst. She was given strychnine and thyroid for these symptoms, with no improvement.

The catamenia had started at eleven years of age followed by considerable dysmenorrhea and irregularity of periods with skipping of three or four months. She had one son, two other pregnancies having ended in miscarriages. The menopause occurred when she was forty-nine years old. The scalp hair on the temples and forehead had been sparse for an unknown period, requiring special care by the hairdresser to mask the deficiency, although there had been no change in texture or curlability. The patient's mother had also had a receding hairline. The patient had had hirsutism of the chin for ten years or more, requiring electrolysis every two months. No change in facial contour had been noted. There was no history of weight loss. Thirteen and eleven years before entry she had an operation for a cataract of the left eye and a repair of an umbilical hernia respectively. At the time of the second operation the urine was normal, and the red-cell count 5,600,000. The nonprotein nitrogen was 22 mg. and the total protein 5.6 gm. per 100 cc., and the chloride 104 milliequiv. per liter.

Physical examination revealed a moderately obese woman, with a somewhat withdrawn appearance in contrast to surprising mental alertness. The face was round, florid and hirsute; the hairline receded markedly. The left eye was totally blind, and the patient could not count fingers with the right. There was periorbital fullness. The neck veins were flat. Peripheral pulsations were good. The chest was clear; there was an apical systolic murmur but no cardiac enlargement. The abdomen was distended and tympanitic. There was questionable ascites. The liver edge, which was smooth, sharp and tender, was palpable 4 fingerbreadths below the costal border. There was ++++ edema of hands, forearms, ankles and legs, and + edema of the abdominal wall. There was an intermittent tremor of the jaw and left leg. The left knee jerk was ++, but the remaining neurologic examination was negative.

The pulse was 110, the respirations 25, and the temperature 99.5°F. The blood pressure was 170 systolic, 100 diastolic.

The urine had a specific gravity of 1.022 and gave a ++ test for albumin, a yellow sugar reaction and a negative reaction for acetone; the sediment contained 3 to 5 white cells, many hyaline casts and a rare cellular cast per high-power field. Examination of the blood revealed a hemoglobin of 12.2 gm. per 100 cc., a red-cell count of 4,120,000, a hematocrit of 29 per cent and a white-cell count of 7500, with 92 per cent neutrophils and 8 per cent lymphocytes. An eosinophil count was reported as 0. The serum potassium was 3.0 milliequiv., the sodium 138.7 milliequiv., the chloride 90 milliequiv., and the carbon dioxide 40.7 milliequiv. per liter; the fasting blood sugar was 317 mg., the nonprotein nitrogen 36 mg., the serum calcium 7.8 mg., the phosphorus 3.0 mg., the alkaline phosphatase 3.2 units, the total protein 4.34 gm., the albumin 2.85 gm. and the globulin 1.49 gm. per 100 cc. The bromsulfalein retention was 42 per cent, and the cephalin flocculation was + in twenty-four and forty-eight hours. The prothrombin time was 15 seconds (normal, 13 seconds), and the blood pH 7.55. A blood bromide determination, blood Hinton test and stool guaiac reaction were negative. An electrocardiogram showed a slight nonspecific abnormality, thought probably to be due to digitalis. A single anteroposterior roentgenogram of the chest taken with the patient recumbent because of poor co-operation showed obliteration of the left costophrenic sulcus by either thickened pleura or fluid and a poorly defined, 3-cm. density projected within the right second interspace, the exact nature of which was not evident (Fig. 1). The heart was at the upper limits of normal in size, and the left ventricle was questionably enlarged. The great vessels projecting along the superior aspect of the mediastinum on the right were somewhat prominent. A single anteroposterior film of the abdomen failed to show any definitely abnormal masses. There was scattered gas in the gastrointestinal tract and extensive calcification of the vessels within the pelvis and along the upper femurs.

FIGURE 1.

In the hospital the patient was treated with digitalis, Mercuhydrin, streptomycin and intravenously administered albumin. However, she became confused and unco-operative and refused to eat. On the fifth hospital day she was much less responsive, and twitchings were more pronounced. She could be roused but was uncommunicative. The lungs were clear, and the heart sounds were unchanged. The edema had disappeared from the arms but was still present in the legs, and there was considerable ascites. The temperature curve showed an irregular, slight elevation. A repeated bromsulfalein test showed 20 per cent retention of the dye in one hour and forty-five minutes. A twenty-four-hour urine specimen contained 2.2 milliequiv. of sodium, 29.2 milliequiv. of potassium and 61 milliequiv. of chloride per liter; it was negative for albumin. The patient became progressively more disoriented and unco-operative, requiring feeding by tube. On the eleventh hospital day the total protein was 4.5 gm., the albumin 3.51 gm., the globulin 1.08 gm., and the nonprotein nitrogen 58 mg. per 100 cc.; the potassium was 3.5 milliequiv., the sodium 140.7 milliequiv., the chloride 88 milliequiv., and the carbon dioxide 42.0 milliequiv. per liter. A twenty-four-hour urine specimen previously sent for 17-ketosteroid determination was at this time reported as containing 43.2 mg. per twenty-four hours.

The problem of nutrition became more acute since the patient refused to swallow, and collapsed veins prevented intravenous maintenance. She died quietly on the seventeenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. ALFRED KRANES*: I am puzzled by the statement that the left knee jerk was ++, which is not abnormal. I suppose it means that the left knee jerk was slightly more active than the right. "On the fifth hospital day. . .twitchings were more pronounced." Nothing was said about twitching before that; this may refer to the tremor of the jaw that was previously described.

May I see the x-ray films?

DR. STANLEY M. WYMAN: The film of the chest taken with the patient lying on her back shows this rather definite density in the right-upper-lung field (Fig. 1). I do not think there is much question that something definitely abnormal is present in the chest; I can debate about what its nature is.

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DR. KRANES: Is this small area the abnormality?

DR. WYMAN: No; it extends as far as the hilus of the lung. It is a mass measuring almost 5 cm. in diameter. The pleural reaction noted on the left may be due to fluid or to old adhesions. I do not see any other intrinsic pulmonary disease or any bone destruction.

DR. KRANES: Is any osteoporosis present?

DR. WYMAN: I do not think there is an unusual amount of osteoporosis for a woman of seventy-six. The film of the abdomen does not show any definite abnormality. There is severe scoliosis of the lumbar spine. The vessel walls are calcified, but I do not see any abnormal masses or unusual enlargement of viscera.

DR. KRANES: Is the skull normal?

DR. WYMAN: Yes; a single film of the skull is normal.

DR. KRANES: When I first read this patient's history, it seemed like that of the usual elderly patient with gradually progressive congestive heart failure, except that the edema of the arms and upper part of the body one month before admission made me wonder whether something more than simple congestive heart failure might not have been present. The staggering episode is puzzling. It may have been due to a cerebrovascular accident, but nothing more is said about it and no specific neurologic changes were described.

A slight seed of suspicion concerning an endocrinologic disorder is planted by the statement that for ten years the patient had hirsutism of the chin, requiring electrolysis every two weeks. That may merely have been a reflection of feminine vanity. The seed is nurtured by the detailed reproductive and menstrual history of a seventy-six-year-old woman. Such details in a person of this age are not usually of any importance and are not included unless relevant. This suspicion of an endocrine disturbance is fortified by the physical examination, primarily by her appearance. It is difficult to visualize people from descriptions. Was a photograph taken of this patient?

DR. HOWARD RASMUSSEN: No.

DR. KRANES: No mention is made about any change in her voice, or of any pelvic examination. I shall assume that the voice had not changed, and that there were no other signs of virilism in the patient — the clitoris was not enlarged, and no pelvic masses were felt.

But it is the laboratory findings that really excite my interest and curiosity. To enumerate them briefly, the patient had diabetes mellitus, there was an eosinopenia (as a matter of fact no eosinophils were found on one examination), and there was a lymphopenia; a hypochloremic hypokaliemic alkalosis was found on two occasions and finally there was a very high 17-ketosteroid excretion in the urine. One has only to enumerate these findings to be reminded that they are highly suggestive, if not pathognomonic, of adrenocortical hyperfunction. These findings, combined with the evidence of the history and the physical examination, make it difficult to escape the diagnosis of Cushing's syndrome. Dr. Fuller Albright used to say that one should not make the diagnosis of Cushing's syndrome in the absence of osteoporosis, but I find it difficult to escape this diagnosis. The duration of the disease is impossible to determine. The facial hirsutism had been noted for ten years; eleven years before, at the time of the second operation, no chemical abnormalities were present, and the patient had no diabetes. If she had Cushing's disease, it began roughly about ten years before admission.

Some of the laboratory findings, which are difficult to reconcile with a diagnosis of Cushing's disease, make me wonder whether something else might not have been present. The serum calcium of 7.8 mg. per 100 cc. is low, but might be explained by the low total serum protein. If Cushing's disease is the result of faulty protein synthesis, one might assume that the low total protein was the result of poor synthesis in a patient with Cushing's disease. Nevertheless, the majority of patients with Cushing's disease do not have a total protein as low as this. It makes me wonder about the presence of complicating disease. Furthermore, there was a marked bromsulfalein retention, to which I shall return in a moment. I am puzzled by the urinary electrolyte studies. There was a striking diminution in the excretion of sodium. It is true that some of the cortical steroids, such as compound E and compound F, cause sodium retention, but I doubt very much if either would give rise to this degree of sodium retention. Desoxycorticosterone causes a much more striking retention of sodium, but it also causes an equal retention of chloride. In the case under discussion there is a marked discrepancy between the sodium and chloride figures. The only way I can put them together is to assume that the patient may have been on a low-sodium diet and may have been given potassium or ammonium chloride or both.

Certainly, some objections to the diagnosis of Cushing's syndrome must have occurred to those who treated the patient as they did to me. The age is very much against Cushing's syndrome, primarily a disease of the first half of life; it occurs in childhood, during adolescence, in the twenties, thirties and occasionally in the forties, but it is very rare in the older age groups. I do not know the age of the oldest patient with this syndrome, but this one was unusually old. The absence of cutaneous striae and bruising are somewhat against it. Striae are not present in all cases of Cushing's syndrome, but they are present in a high percentage. The apparent enlargement of the liver and the laboratory findings suggesting intrinsic liver disease — primarily the low serum protein and marked bromsulfalein retention — are also disturbing. I know

of no bromsulfalein-retention studies on patients with Cushing's syndrome, but I do know that animals given cortisone over an extended period almost invariably have fatty infiltration of the liver. Furthermore, in about half the patients who die with Cushing's syndrome, whatever the cause of death, there is also fatty infiltration of the liver; in some, actual cirrhosis has been described. To be sure, in most cases the cirrhosis is asymptomatic. It is worth while to remind ourselves that the long-continued administration of corticosteroids have the same effect on body tissue as chronic inanition, which sometimes results in fatty infiltration and cirrhosis of the liver. Terminally, the gradually deepening coma and the muscular twitching described suggest that these were due to hepatic coma. I see no way of deciding that question, but these symptoms are rather suggestive. Did this patient receive any ammonium chloride?

DR. RASMUSSEN: I think she received potassium chloride.

DR. DANIEL S. ELLIS: She received ammonium chloride in the last six days.

DR. KRANES: I raise this question because of the interesting paper by Davidson and his group[1] from the Boston City Hospital, describing the production of hepatic coma by administration of ammonium chloride and other nitrogenous substances to people with liver disease. These are not innocuous substances for those who have extensive liver disease. If this patient had cirrhosis of the liver or intrahepatic disease, I think it may well have been the result of Cushing's syndrome.

Having made, to my own satisfaction, a diagnosis of Cushing's syndrome, it next behooves me to try to predict what caused it. Here I am on tenuous ground. There are many causes for the syndrome, and I cannot see how I can choose among them. It may be due to various lesions of the pituitary body, most commonly basophilic adenomas. It has also been described with lesions in the hypothalamus and with hypertrophy or tumor of the adrenal cortex, either benign or malignant. Finally it has been described with ovarian tumors of certain types, and occasionally it has been described when nothing has been found. Of this last group, Dr. Albright says he doubts either the diagnosis or the histology. In this regard I must state — with some reluctance — that in this hospital patients with Cushing's disease have been relieved of their disease by subtotal adrenalectomy, and despite the surgeon's finding of hyperplastic adrenal glands, the pathologist often reports normal adrenal tissue. The histologic technic of identifying adrenal hyperplasia or hyperfunction requires improvement.

In this case there was no evidence of any disease in the pituitary body. Unfortunately, the physician could not examine the visual fields of this practically blind woman. The only suggestion of a central-nervous-system lesion was the episode a month before admission. As between adrenal hyperplasia and tumor, the latter seems more probable because of her age and the suggestion of a metastatic lesion to the lungs. Does that look like a metastasis, Dr. Wyman?

DR. WYMAN: It could be a primary lesion in the lung or could be metastatic.

DR. KRANES: I lean toward carcinoma of the adrenal gland. Whether this was a primary lesion of the lung I see no way of deciding. The patient had certain signs and symptoms that may have been due to superior mediastinal obstruction, — edema of the arms, and the description of the face, — but the neck veins were described as flat. No special difficulties in breathing were noted on physical examination although she had given a history of dyspnea of some ten years' duration. I am not able to say why she had Cushing's syndrome, but suspect an adrenal carcinoma rather than hyperplasia. She may have had some terminal infection, the exact nature of which is not clear. Occasionally in old, debilitated patients one finds so-called marasmic endocarditis on normal heart valves. The fact that she may have had a cerebral embolus a month before admission also suggests this possibility.

DR. JOSEPH C. AUB: Certainly an arrhenoblastoma ought to be seriously considered, particularly at this age.

DR. KRANES: Would that produce all these laboratory abnormalities?

DR. AUB: It is hard to explain the electrolytes on such a basis, but she was probably overventilating, and had diseased kidneys. The increase in male-sex-hormone excretion would produce edema and also would tend to produce cirrhosis and fatty infiltration of the liver; the male hormone does that much more frequently than the female hormone does.

DR. ALLEN G. BRAILEY: Would you think the blindness was in favor of pituitary tumor?

DR. KRANES: I do not see why. I thought it was due to cataracts.

DR. BRAILEY: It became very much worse in the last few weeks of life.

DR. JANET MACARTHUR: I should like to ask Dr. Kranes if he thinks the absence of striae and osteoporosis could have been due to the elevated 17-ketosteroids.

DR. KRANES: That is an interesting suggestion; I had not thought of that before.

DR. FULLER ALBRIGHT: The absence of osteoporosis does not worry me any longer. Contrary to an opinion that I once had, Cushing's syndrome can occur without any demonstrable osteoporosis.

DR. OLIVER COPE: Another condition that I believe might be considered is thymic tumor. Would Dr. Wyman comment upon that? There are 5

well documented cases of Cushing's syndrome associated with tumors of the thymus with no neoplastic changes demonstrable in the adrenal gland. Two of these thymic tumors were described as malignant; at least 2 were described as adrenocortical hyperplasia grossly.

DR. WYMAN: I had not thought of thymus. I cannot exclude it, but from the x-ray appearance I should put it low on the list.

DR. WILLIAM BAKER: A Brazilian physician from São Paulo who was present at the recent research meetings here told me about a patient with a malignant thymoma associated with Cushing's disease. Thymectomy in this patient did not alter the Cushing's disease.

DR. COPE: It was just a suggestion to explain the chest shadow. I suppose it was more probably a metastasis from an adrenal tumor.

DR. ELLIS: I was asked to see this patient primarily because of the large liver. I was trying to explain the heart disease, the liver disease, the pancreatic disease and the renal disease all by one type of disease and wondered whether this was not similar to a case of amyloid disease that was discussed here a year ago. Apparently the onset of the edema and the heart failure was very acute. The patient's daughter, who had gone away believing she was quite well, was called back in a couple of days because of the sudden change in her mother's state of health. I thought she did not have any serious liver disease, because she had a normal albumin-globulin ratio although her total protein was low. If she was having edema and hypoproteinemia on the basis of primary liver disease, I should expect the albumin to have been much lower than it was.

DR. KRANES: It was exceedingly low according to the figures.

DR. ELLIS: But it was in normal ratio.

DR. KRANES: I should think the combination of a very low total protein and the sodium-retaining properties of the adrenocortical hormone could have produced the extensive edema.

DR. ELLIS: We also wondered about widespread metastatic disease of all the organs that have been mentioned, including the adrenal gland and possibly the pituitary body. She was Dr. Rita Kelley's patient; Dr. Kelley is not here. Dr. Rasmussen had occasion to see this patient, and pointed out the symptoms of adrenal hyperfunction.

DR. RASMUSSEN: My opinion, which was not shared by many, was that she had an adrenal-cell carcinoma. My reasoning was much like Dr. Kranes', and I thought the enlarged liver was due to metastases to this organ. Because of her appearance and the hypochloremic alkalosis, we did the urinary 17-ketosteroid determination. We did not receive the report for five days; when the ketosteroids were reported to be high, many other diagnoses were withdrawn.

DR. ELLIS: I did not do a liver biopsy on this patient because the day I saw her she suddenly became critically ill and seemed moribund.

CLINICAL DIAGNOSES

?Adrenal tumor.
?Arteriosclerotic heart disease, with cardiac cirrhosis.
Hypoproteinemia.

DR. ALFRED KRANES' DIAGNOSES

Cushing's syndrome.
Carcinoma of adrenal gland, with metastasis to lung.

ANATOMICAL DIAGNOSES

(Cushing's syndrome), with adrenal hyperplasia.
Carcinoma of lung, oat-cell type, with metastases to pituitary body, pancreas, heart, gall bladder and ovary.

PATHOLOGICAL DISCUSSION

DR. WINFIELD S. MORGAN: At autopsy the peritoneal cavity contained about 500 cc. of clear, serous fluid; the right pleural cavity contained 1000 cc., and the left pleural cavity was obliterated by fibrous adhesions. The liver was not enlarged as we had thought clinically, weighing only 1100 gm. I have no explanation for its being palpable 4 fingerbreadths below the costal border, unless this represented some anatomic variation, nor can I explain the hypoproteinemia or high bromsulfalein retention on the basis of the liver. Grossly, it was not remarkable, and microscopically it showed only mild central congestion; there was no fatty change or cirrhosis. The kidneys weighed 200 gm. and microscopically demonstrated very mild nephrosclerosis. There was a fairly severe acute pancreatitis, with areas of fat necrosis involving all three portions of the pancreas. There was an area of bronchopneumonia, with abscess formation in the right lower lobe. The heart weighed 340 gm. and showed slight hypertrophy of the left ventricle. The valves were normal, and microscopically no intrinsic myocardial disease was found.

In the region of the right-upper-lobe bronchus at its orifice a tumor surrounded the bronchus, replacing the wall but extending only for a short distance into the lung substance. Microscopically, it proved to be a carcinoma of the oat-cell type. It did not have the appearance of a thymoma. Single metastases were present in the posterior lobe of the pituitary body, the anterior portion of the interventricular septum of the heart, the fundus of the gall bladder, the pancreas and the right ovary. With the exception of the right ovary, which measured 4 cm. in greatest dimension, the other metastatic lesions measured 1 cm. or less. The tumor in

the ovary was similar to the other metastases and did not look like a primary tumor such as an arrhenoblastoma.

The adrenal glands weighed 38 gm. and were symmetrical, with finely nodular cortical surfaces. On section they presented a firm cut surface, which was predominantly bright yellow. Microscopical examination showed a cortical hyperplasia, with cells that were large and polyhedral, some having clear cytoplasm and others having a faintly acidophilic cytoplasm. I thought there was considerable atrophy of the zona glomerulosa with the hyperplasia confined to the other two zones.

Sections of the spine did not show any significant amount of osteoporosis that might not be compatible with the age of seventy-six.

Examination of the brain did not reveal any lesion that might have accounted for the episode of giddiness and staggering that occurred one month before admission to the hospital.

I think that the immediate cause of death aside from the terminal problem of nutrition was the acute pancreatitis and the bronchopneumonia.

Dr. Burt and Dr. Cohen have carried out special studies on the pituitary body and adrenal glands, and I shall ask them to present their findings at this time.

DR. AGNES S. BURT: The pituitary body weighed 83 mg. after fixation, which is near the upper limit of the normal range for this laboratory. On section the entire increase in size was seen to be due to metastatic carcinoma confined to the posterior lobe. The anterior lobe contained no metastases and no adenomas of any description. The gland was studied histologically by the periodic acid Schiff (PAS) reaction with an orange G counterstain and a differential count performed on 2940 cells from three widely spaced sections according to the method of Rasmussen and Herrick.[2] Six cell types were differentiated as follows: *normal basophils* (NB), rounded or oval cells densely packed with PAS-positive granules that correspond to the beta cells of Romeis[3]; *hyaline basophils* (HyB), which show areas of clear, salmon-pink cytoplasm after the PAS reaction, are apparently derived from normal basophils and are thought by Crooke[4] to be pathognomonic of adrenal hyperactivity; *sparsely granulated basophils* (SGB), large, usually polygonal, cells containing irregularly distributed clumps of PAS-positive granules that we believe correspond to the delta cells of Romeis[3] (Mellgren[5] has reported that these cells often increase significantly in Cushing's syndrome and adrenogenital virilism); *hypertrophic amphophils* (HA), which have giant, frequently bilobed, nuclei and variable amounts of foamy cytoplasm in which no specific granules can be demonstrated by the PAS reaction — they are clearly derived from the sparsely granulated basophils and, like hyaline basophils, increase significantly in states of adrenal hyperactivity[5]; *acidophils* (Ac), which are easily differentiated by abundant small granules that stain intensely with orange G; and *chromophobes* (Chr). All cells not falling into one of the categories listed were classified as chromophobes.

Table 1 shows the result of the count in this patient as compared with the average for 11 endocrinologically normal postmenopausal women whose pituitary bodies have been studied by the same method.[6]

TABLE 1. *Differential Count (Anterior Pituitary Body), PAS Orange G Preparations.*

SUBJECT	NB	HyB	SGB	HA	Ac	Chr
	%	%	%	%	%	%
Present case	5.4	8.3	11.5	4.3	33.1	37.2
Average of 11 normal postmenopausal women	10.5	—	5.5	0.9	33.4	49.7
Standard deviation	3.50	—	1.41	0.34	5.93	3.89

Hyaline basophils, sparsely granulated basophils and hypertrophic amphophils, all forms that other investigators have found to increase in adrenal hyperactivity, were significantly elevated in this woman. Normal basophils were well within the normal range. It is interesting that, although the patient died with an active carcinoma, the acidophils, which presumably secrete growth hormone, were neither quantitatively nor qualitatively abnormal.

DR. RICHARD B. COHEN: The adrenal findings were in accord with Dr. Burt's findings in the pituitary body. There was a marked hyperplasia of the adrenal cortex. No line of demarcation could be determined between the reticulosa and fascicularis. The cells were large and polygonal, contained a granular acidophil cytoplasm and were sparsely vacuolated. There was a considerable proportionate reduction of sudanophilic material throughout the

hyperplastic zone. The Schultz modification of the Liebermann-Burchard reaction and the Windaus reaction, which demonstrates cholesterol and cholesterol-like substances, revealed a marked reduction of these substances in the cortex. The Ashbel-Seligman reaction, which is designed to demonstrate active ketonic carbonyl groups, showed some patchy staining in the inner and mid-cortical zones, but this was scant. Birefringent material was reduced.

I think this pattern would fit in very well with that of an active adrenal gland — actively secretory, without appreciable storage taking place.

It should be pointed out that the reactions carried out are not entirely specific and that this fact must be taken into consideration in the interpretation. These histochemical findings should be correlated with clinical and laboratory data before they can be properly interpreted.

DR. COPE: This discussion of the histologic details of both the anterior pituitary body and the adrenal cortex is very heartening because it denotes great progress. The major trouble in the understanding of the pathology of the Cushing syndrome, as Dr. Kranes has intimated, has been to identify cortical hyperplasia. We, as surgeons, think we have been able to see it on gross examination, but it has not been possible until very recently for you, as pathologists, to give any lead concerning whether we have been right or not. I consider this last report of Dr. Cohen as an excellent contribution. The absence of a pituitary adenoma is equally important in our understanding of the pathology.

DR. COHEN: The utilization of the histochemical technics might be particularly valuable in adrenal glands that present no gross or microscopical evidence of tumor or hyperplasia to account for pronounced clinical symptoms of the Cushing or adrenogenital syndrome. We have not examined any of these yet.

DR. COPE: One might stress the fact that if the adrenal glands weighed 38 gm. considerable hyperplasia must have been visible on gross examination.

DR. MORGAN: That is about three times the normal weight.

DR. KRANES: I should like to ask about the ages of the patients with Cushing's syndrome. How old was the oldest?

DR. JOHN W. RAKER: The oldest patient in our hospital series was sixty-two years.

DR. MORGAN: We do not know just what relation this patient's endocrine abnormalities had to the terminal carcinoma; however, there is some evidence in the literature that the simultaneous occurrence of the two diseases may have been more than coincidence. Adrenal dysfunction[7] and abnormal excretion of alpha ketosteroids[8] have been reported in a wide variety of human cancers, and cortisone has been found to promote the growth of transplanted sarcomas in animals, possibly by reducing the immunity of the host.[9] In view of the current interest in the effect of bilateral adrenalectomy on inhibiting tumor growth, we thought that this case might be of significance in showing the reverse side of the coin.

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BAKER'S DOZEN 1953

THE current issue of the *Journal*, introducing Volume 248 to a breathlessly expectant public, bears the date January 1, regardless of when it may actually reach that public. For there's many a slip twixt the editorial office and the postman's sack, and New Year's Day is one on which many of the Workers of the World refrain from working. By the same happy coincidence the final issue of Volume 247 bore the date of Christmas Day and was no doubt similarly uncertain in regard to its arrival in the letter boxes of this and other countries.

The publication of the *Journal* on the two happiest holidays of the year is a not entirely unexpected occurrence, however, for it happens approximately every seven years except for some slight confusion attributable to the occasional insertion of an extra day in February. An important by-product of this rotatory action of days and dates is the appearance of fifty-three Thursdays in 1953 and consequently the issuance of fifty-three numbers of the *Journal*, at no extra cost to the subscribers.

The same thing, unfortunately, cannot be said for the *Journal's* publishers and proprietors. This issue is paid for, promptly, like all the others, and distributed among the subscribers in a magnanimous gesture of good will and with a ringing "Happy New Year!" By the same token 1953 is, incidentally, an excellent year for new subscribers, if they are interested in such bargains.

MEASURING THE SUBJECTIVE RESPONSE

MOST of the familiar experimental work in pharmacology has depended on the measurement of objective responses to drugs, and useful and accurate results have been obtained. In these investigations the animals lower than man have been employed in the testing, and have proved to be generally satisfactory when phenomena that can be measured objectively are to be observed.

When attention turns to the more delicate quantitation of *subjective* responses, however, on which little work has so far been performed, man, as Beecher* points out, is the "animal of necessity." It furthermore becomes obvious, as one follows the methods and technics that Beecher and his coworkers have devised, that more and more of the experimental biochemistry, physiology and pharmacology of the future will be studied with man as the subject.

With such subjective factors as headache, fatigue, tension, relaxation and pain conceivably to be used as the sensations on which responses are to be measured, entirely new and most careful technics and methods of observation and calibration must be employed. Precise work in such a field may well be of as much value to the psychiatrist, seeking a scientific approach, as to the pharmacologist; the psychiatrist, in fact, may eventually be found quantitating such vital emotions as sorrow and

*Beecher, H. K. Experimental pharmacology and measurement of subjective response. *Science* 116:157-162, 1952.

happiness in carefully calibrated degrees of melancholy or of euphoria.

The more elusive the responses to be measured, the more rigid the controls must be; where the effects of the applied factor are so difficult to measure as they are in subjective responses, the standards of measurement must be as firmly established as possible. With these requirements satisfactorily fulfilled, Beecher finds that the same acceptable degree of accuracy — within an 8 per cent error — can be attained in measuring subjective as in measuring objective responses.

At least in the preliminary stage of such experimentation, pain appears to be the sensation most adaptable for use in measuring man's response to pharmacologic control. Investigations so far conducted have shown, moreover, that in measuring the power of an agent in relieving pain, *natural* pain must be used as the sensation of choice and not pain artificially produced. The various emotional factors, too, that may invalidate the experiment must be taken into account.

The criteria for establishing satisfactory controls, the basis of all successful experimentation, have been carefully determined. A strictly neutral attitude in eliciting responses is necessary, which presupposes ignorance of the terms of the experiment on the part of both subject and investigator. Neutrality in the design of the experiment is essential, with a technic of utter random selection, the employment of control substances such as placebos or already standardized drugs being interspersed at random with the unknown factor to be tested. In the use of placebos, account must be taken of the possibility that a certain proportion of persons who are "placebo reactors" may be encountered. Subjects must be willing, co-operative and undistracted — and preferably males, since the menstrual cycle and other factors may influence the response of women.

Lest, by the removal of selected statements from their context, any persons should leap to the conclusion that all experimentation on animals has been and will forevermore be useless, it must be emphasized that even in this unique type of investigation the lower animals are essential for the primary screening. Man is the animal of necessity only in the final stages of experimentation.

MEDICAL EDUCATION AND THE COMMONWEALTH FUND

The Commonwealth Fund, founded October 17, 1918, by Mrs. Stephen V. Harkness "To do something for the welfare of mankind," has recently issued its thirty-fourth annual report. In this statement the Fund, one of America's truly great philanthropic institutions, expresses the need for a better understanding and a greater encouragement of the changes for the better that are going on in medicine; in particular those related to medical education and the evolution of health services.

Of the three factors that influence the shape and direction of medical progress — the school, the profession and the recipients of medical care — the school is the one at present in the best position to guide the others and consequently to influence the future development of medicine. Education, rigid as it may be in its details, is fortunately in its broadest sense relatively plastic. Its greatest handicap lies in the tendency of teaching to become formalized; its greatest safeguard is the refusal of learning to follow beaten paths.

It is here that the Fund is most interested in helping to develop the way — "to shift the emphasis from teaching to learning, from the department to the school, and from the specialty to the patient." Even as long ago as the well known pilgrimage to Canterbury, when Chaucer's clerk would gladly learn and gladly teach, the learning has at least at times seemed to have taken precedence over the teaching.

Education, with its emphasis on learning more than on teaching, must become comprehensive rather than engrossingly scientific, adopting a holistic concept of its responsibilities to the individual and the community, in sickness and in health. Research must turn from a complete preoccupation with the scientific problems of medicine to the problems of its application, putting its greatest efforts into finding the means of laying the offerings of medicine at the service of those who need them. Here, regardless of the phraseology, are the present and future problems of medical education and medical practice, in which the Commonwealth Fund is interested.

Its interest, of course, has taken a most tangible form. In 1950 a five-year grant was made to Western

Reserve University School of Medicine to reorganize its curriculum, which has taken the direction of dividing its four-year span into 3 phases. The first orients the student to medicine *and to the patient*; the second introduces disease, like the serpent in the Garden of Eden; the third deals with the care of sick people — and, it may be hoped, well ones also.

An appropriation has been made to the division of medical sciences of the Graduate School of Arts and Sciences at Harvard for work along similar lines, and other grants have been made to the Cornell University Medical College, the College of Medicine of the University of Tennessee, the Peter Bent Brigham Hospital, the University of Florida, Columbia University and the schools of medicine of the universities of Colorado, Louisville, and Pennsylvania, Boston University and Yale University.

This is but a partial list of the projects that the directors of the Commonwealth Fund, with great care and forethought, are implementing "To do something for the welfare of mankind."

WHITE-COLLAR WORKERS

THE *British Medical Journal* for October 18, 1952, comments on the disturbance occasioned in academic circles in 1950 when the Ministry of Labour announced an impending five-year overproduction of biologists in the United Kingdom. The delayed reaction to this announcement has been a recent symposium on biology as a career, conducted by the Institute of Biology at the University of Birmingham.

The picture turned out to be not as black as originally painted, for the Technical and Scientific Register of the Ministry showed, by quoting figures of recruitment to the scientific offices class of the Civil Service, "that there is as good a market for honours graduates in botany, zoology, and physiology as there is for those in chemistry." Unfortunately for the long-term purity of pure science, biology is frequently recommended as a fit subject for students who are no good at physics or mathematics. One is reminded of the local high-school student(?) of a not too remote generation who, being unable to meet the requirements for college, was advised to take up medicine, which he did, with no conspicuous lack of success.

Fortunately for the continued prosperity of teaching in biology, it has been found that biologists take easily to administration, a useful career into which the stream of excess biologists can be diverted.

Smallpox has made its way into western Vermont. — A war has been commenced against pessaries. — What is thought of filling teeth with a solution of gum shellac? — Several new medical works are in progress.

Boston M. & S. J., *January 5, 1853*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

DUNN — Joseph H. Dunn, M.D., of Rockland, died on November 16. He was in his sixtieth year.

Dr. Dunn received his degree from Tufts College Medical School in 1916. He was chairman of the Rockland Board of Health and a member of the American Association of Industrial Physicians and Surgeons.

He is survived by his widow, two sons, a sister and two brothers.

GARLAND — Marion C. Burrows Garland, M.D., of Monson, Maine, died on November 13. She was in her eighty-second year.

Dr. Garland received her degree from Tufts College Medical School in 1906. She was formerly an official of the Lynn Health Department and city physician of the Lynn Contagious Hospital and was a former member of the Massachusetts Medical Society.

She is survived by a nephew.

LIA — Bianca R. Lia (Gordon), M.D., of Arlington, died on November 15. She was in her forty-fifth year.

Dr. Lia received her degree from University of Pittsburgh School of Medicine in 1932. She was chief of radiology at the New England Hospital and a member of the New England Roentgen Ray Society and a fellow of the American College of Radiology.

She is survived by her husband.

WELLS — Charles E. Wells, M.D., of Randolph, died on November 13. He was in his seventy-fifth year.

Dr. Wells received his degree from the University of Vermont College of Medicine in 1908. He was formerly assistant director of the Massachusetts General Hospital and superintendent of the Woonsocket (Rhode Island) Hospital and was school physician in Randolph.

He is survived by two sons, a daughter and four grandchildren.

WHEELER — Lucia A. Wheeler, M.D., of Uxbridge, died on November 25. She was in her eighty-fourth year.

Dr. Wheeler received her degree from Woman's Medical College of Philadelphia in 1898. She received a medal for fifty years' membership in the Massachusetts Medical Society last year and was a fellow of the American Medical Association.

She is survived by two sisters.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

REVIVAL OF "SANITALK"

"Sanitalk," a quarterly publication of the Division of Sanitary Engineering of the Department of Public Health, was revived and issued in a greatly improved form beginning with the November, 1952, number. The publication was begun shortly before World War II and eventually became a victim of the shortages of that period.

Its purpose is to acquaint water-works and sewerage-works officials and others with latest developments in the field of environmental sanitation. It will serve as a means of communication, within the circle of the sanitary sciences of biology, chemistry and engineering, concerning the latest research activities at the Lawrence Experiment Station, which will move into its new building about August, 1953.

The publication will serve as a news contact between the Department of Public Health and the broad field of environmental sanitation, including certain parts of the civil defense program.

The "Sanitalk" mailing list will include water and sewer departments in Massachusetts, members of the Conference of State Sanitary Engineers and numerous college and university libraries in the United States.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

The January schedule of the Consultation Clinics for Crippled Children in Massachusetts is as follows:

Orthopedic Clinic	Date	Clinic Consultant
Salem	January 5	Paul W. Hugenberger, M.D.
Gardner	January 6	Carter R. Rowe, M.D.
Haverhill	January 7	William T. Green, M.D.
Greenfield	January 8	Charles L. Sturdevant, M.D.
Brockton	January 8	George W. Van Gorder, M.D.
Lowell	January 9	Albert H. Brewster, M.D.
Worcester	January 9	John W. O'Meara, M.D.
Lynn*	January 12	Daniel M. Killoran, M.D., and John J. Crowley, M.D.
Hyannis	January 15	Paul L. Norton, M.D.
Fall River	January 19	David S. Grice, M.D.
Springfield	January 20	James D. Fisher, M.D.
Pittsfield	January 21	Edward J. Coughlin, Jr., M.D.

Rheumatic-Fever Clinic	Dates
North Reading	January 6, 13, 20, 27
Fitchburg	January 7, 14, 21, 28

Plastic Clinic	Held	Consultant
Eastern Massachusetts	Semi-monthly	Bradford Cannon, M.D.
Western Massachusetts	Monthly	Joseph M. Baker, M.D.

Physicians referring new patients to clinic should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

*This clinic serves Lynn, Lynnfield, Saugus, Nahant, Revere, Chelsea, Everett and Winthrop. Referrals should be made directly to the Lynn Hospital.

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR NOVEMBER, 1952

Résumé

Disease	November 1952	November 1951	Seven-Year Median
Chancroid	0	1	2
Chicken pox	1250	658	1450
Diphtheria	0	6	21
Dog bite	624	662	616
Dysentery, bacillary	17	1	4
German measles	62	96	64
Gonorrhea	126	180	257
Granuloma inguinale	0	0	0
Lymphogranuloma venereum	0	0	0
Malaria	5	131	1
Measles	83	861	702
Meningitis, meningococcal	4	10	9
Meningitis, Pfeiffer bacillus	5	2	8
Meningitis, pneumococcal	1	3	3
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	0	0	0
Meningitis, undetermined	7	5	4
Mumps	420	1061	847
Poliomyelitis	22	12	11
Salmonellosis	14	11	4
Scarlet fever	208	141	475
Syphilis	130	185	238
Tuberculosis, pulmonary	198	160	207
Tuberculosis, other forms	7	7	12
Typhoid fever	1	2	2
Undulant fever	2	0	2
Whooping cough	101	297	448

Comment

Diseases below the seven-year median were chicken pox, diphtheria, measles, meningococcal meningitis, mumps, scarlet fever and whooping cough.

For the fifth consecutive month no cases of diphtheria were reported.

The eighty-three cases of measles reported represented the lowest figure for November since 1906.

With but one exception, the 203 cases of scarlet fever made this the lowest figure for the month of November in any year in Massachusetts.

Whooping cough reached the lowest figure (101 cases) ever reported for November in the State.

Diseases above the seven-year median were bacillary dysentery, poliomyelitis and salmonellosis.

The incidence of bacillary dysentery and salmonellosis was the highest for the month of November since 1947 and 1946 respectively.

Geographical Distribution of Certain Diseases

The following diseases were reported from the communities named:

Dysentery, bacillary: Boston, 1; Grafton, 1; Waltham, 3; Wrentham, 12; total, 17.

Hepatitis, infectious: Boston, 4; Chicopee, 2; Fall River, 1; Fort Devens, 2; Millbury, 5; Pittsfield, 1; Worcester, 24; Wrentham, 56; total, 95.

Malaria: Fort Devens, 5.

Meningitis, meningococcal: Boston, 1; Lawrence, 1; Weymouth, 1; Woburn, 1; total, 4.

Meningitis, Pfeiffer bacillus: Boston, 1; Lowell, 1; Lynn, 1; Pittsfield 1; Warwick, 1; total, 5.

Meningitis, pneumococcal: Everett, 1.

Meningitis, undetermined: Boston, 1; Cambridge, 1; Pittsfield, 1; Somerville, 1; Springfield, 1; Worcester, 2; total, 7.

Poliomyelitis: Amesbury, 1; Boston, 1; Brookfield, 1; Hampden, 1; Haverhill, 1; Holyoke, 1; Lawrence, 1; Leominster, 1; Lowell, 1; Lunenburg, 2; Malden, 2; Marblehead, 1; North Brookfield, 1; Oxford, 1; Salem, 1; Somerville, 1; Wellesley, 2; West Brookfield, 1; total, 21.

Salmonellosis: Beverly, 3; Boston, 1; Marblehead, 1; Milton, 1; Needham, 1; Reading, 1; Somerville, 1; Springfield, 1; Waltham, 1; Watertown, 1; Wellesley, 1; Worcester, 1; total, 14.

Septic sore throat: Boston, 1; Cambridge, 1; Franklin, 1; Marblehead, 1; total, 4.

Trichinosis: Salem, 1.

Typhoid fever: Everett, 1.

Undulant fever: Rehoboth, 1; Southbridge, 1; total, 2.

CORRESPONDENCE

A MAN'S A MAN FOR A' THAT

To the Editor: King, in the Medical Progress report on tuberculosis in the November 6 issue of the *Journal* states that "The Veterans Administration series reported in January, 1951, shows that of 80 patients with meningitis (without miliary disease) who were checked at the end of twenty-four months only 11 per cent were living."

Just how many are 11 per cent of 80 patients? Perhaps 0.2 of one of the patients had died and has been amputated from the remainder that still lived?

R. L. SWARM, M.D.

St. Louis, Missouri

Note: The division of patients does seem odd, but coming from such an unimpeachable source as the Veterans Administration it was, of course, not questioned. — ED.

NEED FOR A BETTER LAW

To the Editor: I am writing about the leading editorial in the October 2 issue of the *Journal* entitled "Call to Active Duty," hoping it will clarify the situation.

Several provisions of Public Law 779 are apparently disregarded by the writer of this editorial. The first is, that the law sets up a definite priority of call in four priorities for supplying the needed health personnel in the mobilization effort. The second is that the law clearly defines a limit of service at which time a man must be replaced. Since these men entered service throughout the course of twelve-month periods and serve a maximum of twenty-four months, they must be replaced at that time and not months later when a hospital year terminates.

Furthermore, all hospitals were notified last February in a bulletin issued by the National Advisory Committee to the Selective Service System that they should select their hospital staffs first from Priority IV; then from Priority III, with the older physicians first; then from Priority II with those with the most service first; and finally, in rare cases, physicians in Priority I.

It is legally impossible and morally wrong to keep the men longer than their two years of service for the convenience of hospitals.

We call these statements to your attention, hoping it will provide a better understanding of the programing under the provisions of Public Law 779.

National Advisory Committee to the Selective Service System — HOWARD A. RUSK, M.D., *Chairman*

Note: It is difficult to concede that the needs of the military services must, during a limited emergency, disrupt civilian health and educational programs. Proper planning in utilizing the pool of available physicians and *sufficient* notice to prospective inductees before the time when annual appointments in civilian hospitals customarily begin could fulfill the requirements of both military and civilian needs without doing injustice to anyone. It is hoped that the new law will be so framed and executed as to embody this general principle. — ED.

ACADEMY OF GENERAL PRACTICE

To the Editor: Recalling our conversation on the evening of September 24 I am pleased and gratified that the October 23 issue of the *Journal* carried a most concise and eloquent editorial concerning the Academy of General Practice. The warmth of feeling between the official body of the Academy and the older organizations of which we are proud to be members is further strengthened by such a gesture on your part. It makes us believe that as the younger brother in medical organizations we are being aided and encouraged by our elder brothers. Such a co-operative gesture makes us more firmly resolved to be in all our efforts all that you would expect us to be.

I am also happy to have recognized the strong and excellent leadership of Dr. Harvey A. Kelly, whose wise and conservative counsel is of inestimable value to any organization. He has been unstinting in his time and effort to make the year of his leadership of the Massachusetts Chapter a success and the conservative growth during his leadership, together with the two splendid meetings he engineered, is ample testimony of this fact.

As always, your concise editorials add stature to the always good *New England Journal of Medicine.*

JOHN R. FOWLER, M.D.

American Academy of General Practice
Barre, Massachusetts

PHILADELPHIA PATHOLOGICAL SOCIETY

To the Editor: May I call your attention to an omission in the editorial on pathology in the November 13 issue of the *Journal?*

The Philadelphia Pathological Society, which is still flourishing, was founded in 1857, though it is true that an earlier one — founded in 1839 — lasted only a few years. Doubtless, other local societies could be found that began between 1857 and 1900, when the American Association of Pathologists and Bacteriologists was founded.

Your editorials are always interesting and so seldom inaccurate that I considered this to be worth bringing to your attention. Perhaps it was the secretary of the College of American Pathologists who first made the slip.

E. B. KRUMBHAAR, M.D.

Philadelphia, Pennsylvania

ANOTHER PENICILLIN REACTION

To the Editor: I was much interested in the paper by Drs. Higgins and Rothchild on the subject "Fatal Anaphylactic Shock from Procaine Penicillin," which appeared in the October 23 issue of the *Journal.* This case report brings to mind another "penicillin reaction" — namely, the Jarisch–Herxheimer reaction described by Bauer and Egolf, in an article entitled "Herxheimer Syndrome Following Penicillin in Unsuspected Syphilis" (*Bull. Army M. Dept.* 4:239, 1945). The 2 patients described by us developed a reaction within hours of the injection. One went into peripheral vascular collapse.

F. K. BAUER, M.D.
Director, Radioisotope Unit

Veterans Administration Center
Los Angeles, California

MASTECTOMY, FORSOOTH

To the Editor: In the November 27 issue of the *Journal* an editorial appears entitled "Amazonia." I started reading this, expecting to find an account of the surgical treatment of carcinoma of the breast — possibly another critique of the work of MacWhorter, or some article discussing the end results in another 500 cases. I found, to my surprise, that this is a discussion of the dwindling male population. This raises certain matters of etymologic interest that I am sure should be gone into in great detail.

The word "amazon" comes from the Greek root a-mazos and means "without a breast." The root -maz or -mas is of course employed in such medical terms as mastectomy, gynecomastia and mazoplasia.

According to mythology, there dwelt in Asia Minor a group of women warriors whose chief weapon was the bow and arrow. Since they wore little clothing, it is quite clear that a full-bosomed, right-handed woman warrior might find that the right breast got in the way when the bowstring was released. Therefore, the breast was removed. As a result, this absence of the right breast became the identifying symbol of a warlike group of women. Hence, the term "amazon."

There are those who, contrary to this reasonable discourse, stoutly maintain that the word amazon refers to any woman whatsoever, and comes from the same root as the word *amaze.* Clearly, such a theory is not worth further discussion.

Returning now to the true derivation, one finds that the *Encyclopedia Britannica,* — that source of all truth, — in discussing the Amazons, omits completely this interesting derivation of the word. Despite this omission in the text, the famous statue of the Amazon found in the Vatican museum at Rome is depicted. This statue clearly shows a woman warrier with a broken bow and a broken arrow. The statue is missing the right breast, and the encyclopedia misses the point.

Even Webster's dictionary, although it gives minor recognition (in fine print at the bottom of the page) to the essential surgical derivation of the word *amazon*, sees fit to omit this delicate matter from the main dictionary text.

The mythical amazons consorted with males but once a year. At an appropriate time thereafter they slaughtered all the male offspring. In a sense, then, it might be appropriate to use this term with reference to female preponderance in the population. But there is no avoiding the fact that its true meaning is of surgical import and relates to a warlike female race in whom unilateral mastectomy has been performed for reasons of ordnance.

FRANCIS D. MOORE, M.D.
Boston, Massachusetts

Note: Dr. Moore fails to take into consideration the predicament in which a left-handed female archer would find herself, with the right breast removed; he fails also to discuss the root "max" with a slightly different spelling and definition — that is, maize = corn. — ED.

MISCELLANY

FREDERICK H. VERHOEFF FELLOWSHIP

The ophthalmic staff of the Massachusetts Eye and Ear Infirmary has set up a fellowship in honor of Frederick H. Verhoeff. The support of the Fellowship will come chiefly from a fund amounting at present to approximately $60,000 that has been collected by the staff. The income will be used to make grants for research and study at the Massachusetts Eye and Ear Infirmary. The grants will be administered by a committee chosen annually by the staff.

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

The following officers of the New England Obstetrical and Gynecological Society have been elected for the year 1953: president, Dr. Joel M. Melick, 27 Elm Street, Worcester, Massachusetts; vice-president, Dr. Edward F. Shay, 450 Hood Street, Fall River, Massachusetts; treasurer, Dr. Frederick L. Good, 20 Commonwealth Avenue, Boston; secretary, Dr. Carmi R. Alden, 270 Commonwealth Avenue, Boston; and chairman of the Council, Dr. Lewis P. James, 350 Farmington Avenue, Hartford, Connecticut.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Signs and Symptoms: Applied pathologic physiology and clinical interpretation. Edited by Cyril M. MacBryde, M.D., associate professor of clinical medicine, Washington University School of Medicine, assistant physician, Barnes Hospital, and director, Metabolism and Endocrine Clinics, Washington University Clinics, St. Louis, Missouri. Second edition. 8°, cloth, 783 pp., with 98 illustrations, 50 charts and 8 color plates. Philadelphia: J. B. Lippincott Company, 1952. $10.00.

This second edition of a book first published in 1947 has been thoroughly revised, and chapters have been added on pathologic bleeding, pigmentation of the skin, vertigo and dizziness, and on clubbed fingers and osteoarthropathy. Lists of selected references are appended to the various chapters, there is a good index, and the publishing is well done.

Fundamentals of Psychiatry. By Edward A. Strecker, M.D., Sc.D., LL.D., Litt.D., professor of psychiatry and chairman, Department of Psychiatry, Undergraduate and Graduate Schools of Medicine, University of Pennsylvania, psychiatrist to the Pennsylvania, Philadelphia and Germantown Hospitals, and consultant and chief-of-service, Institute of the Pennsylvania Hospital, and consultant to the Surgeons General, United States Army and United States Navy. Fifth edition. 8°, cloth, 250 pp., with 21 illustrations. Philadelphia: J. B. Lippincott Company, 1952. $4.50.

In view of the fact that the field of psychiatry is urgently in need of personnel, this new edition of a standard work is addressed especially to the general practitioner. A chapter on psychotherapy has been added, and the chapter on psychosomatic medicine and psychiatry has been completely rewritten.

NOTICES

SOUTH END MEDICAL CLUB

A luncheon meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, January 20 at 12 noon. Dr. Nicholas J. Fiumara, director of the Division of Venereal Diseases, Massachusetts Department of Public Health, and lecturer in dermatology and syphilology at Tufts College Medical School, will speak on the subject "Modern Methods in the Diagnosis and Treatment of Gonorrhea and Syphilis."

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

A meeting of the New England Society of Physical Medicine will be held at the Massachusetts General Hospital, Boston, on Wednesday, January 21, at 8 p.m. A symposium on arthritis will be held, the speakers being Hans Waine, M.D., medical director, New England Chapter of the Arthritis and Rheumatism Foundation; Charles L. Short, M.D., associate physician, Massachusetts General Hospital, and member, Arthritic Clinic; and Arthur L. Watkins, M.D., chief of physical medicine, Massachusetts General Hospital, and assistant clinical professor of medicine, Harvard Medical School.

Physicians, rehabilitation personnel and students are cordially invited to attend.

FIRST PUBLIC HEALTH WORKSHOP ON DENTAL CARE IN INDUSTRY

The First Public Health Workshop on Dental Programs in Industry will be held at the Hotel Statler, New York City, on Friday, January 30. The Workshop will deal with contemporary dental-care problems in industry, and will be discussed in three panels to be held in the morning and the afternoon, concluding with an evening lecture on medical-dental co-operation.

HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society will be held in the main amphitheater of the Peter Bent Brigham Hospital on Tuesday, January 13, at 8 p.m., with Dr. Francis D. Moore presiding.

PROGRAM

Problems Relating to Transplantation of the Kidney in Man. Benjamin Miller, David Hume, Arnold Colodny, John Merrill and George W. Thorn.

Experiences with the Treatment of Renal Failure in Korea. Lloyd H. Smith, Paul E. Teschan, Robert S. Post and John M. Howard.

Vascular Injuries in the Korean War. Major Edward J. Jahnke, USAF (MC).

The Relation of Antigen Catabolism to Visceral Lesions. Gustave Dammin and F. G. Germuth.

Metabolic Changes Following Mitral Surgery. Laura Brooks, Graham Wilson, Isidore S. Edelman, Allan Myrden, Lewis Dexter, Dwight Harken and Francis D. Moore.

HARTFORD MEDICAL SOCIETY

The Program Committee of the Hartford Medical Society announces the following series of lectures, which will be given during the early months of 1953. The fall series of lectures will be announced later. All lectures will be held on Mondays at 8:30 p.m., in the Hunt Memorial Building, Hartford, Connecticut, and will be preceded by a clinical conference held at one of the local hospitals at 5 p.m.

Program

January 19. The Practical Use of Antibiotics. Chester S. Keefer, M.D., of Boston.
February 2. Practical Consideration of Breast Tumors. C. F. Geschickter, M.D., of Washington, D. C.
February 16. Low Back Pain. Joseph S. Barr, M.D., of Boston.
March 2. Thromboembolic Disease. Jere W. Lord, Jr., M.D., of New York City.
March 16. Practical Considerations of Fluid Therapy. Thaddeus S. Danowski, M.D., of Pittsburgh, Pennsylvania.
April 6. Surgery for Peptic Ulcer, with or without Vagotomy. John H. Garlock, M.D., of New York City.
April 20. Differential Diagnosis of Jaundice and Application of Liver-Function Tests. Harold Jeghers, M.D., of Washington, D. C.

AMERICAN COLLEGE OF SURGEONS

An attractive program of papers, panels and symposiums will be offered at the sectional meeting of the American College of Surgeons to be held at the Atlanta Biltmore Hotel, Atlanta, Georgia, February 23 and 24. William G. Hamm, M.D., of Atlanta, chairman of the Committee on Arrangements, has collaborated with the Georgia Chapter of the College in planning the meeting. An added feature is the concurrent Atlanta Postgraduate Medical Assembly, to which sectional-meeting visitors are cordially invited. There will be three joint sessions of the Assembly and College meetings.

SOCIETY MEETINGS AND CONFERENCES

January 3–31. Springfield Hospital Educational Program. Page 1000, issue of December 18.

January 3–June 2. Mount Auburn Hospital Panel Discussions. Page 868, issue of November 27.

January 5. New England Cardiovascular Society. Page 1001, issue of December 18.

January 7–28. Lahey Clinic Lectures. Page 1050, issue of December 25.

January 7–April 1. Massachusetts Medical Society. Postgraduate Medical Institute Course in General Medicine. Page 1050, issue of December 25.

January 7–April 8. Postgraduate Medical Institute. Page 452, issue of September 18.

January 9. Massachusetts Society of Anesthesiologists. Page 1050, issue of December 25.

January 9–30. Combined Anesthesia Teaching Conferences of Boston. Page 785, issue of November 13.

January 12–March 23. Postgraduate Course in General Medicine. Page 697, issue of October 30.

January 13. Springfield Academy of Medicine. Page 1001, issue of December 18.

January 13. Harvard Medical Society. Page 41.

January 14. Essex North District Medical Society. Page 743, issue of November 6.

January 19–April 20. Hartford Medical Society. Notice above.

January 20. South End Medical Club. Page 41.

January 21. Boston Graduate Club of Phi Delta Epsilon Medical Fraternity. Page 1050, issue of December 25.

January 21. New England Society of Physical Medicine. Page 41.

January 30. First Public Health Workshop on Dental Care in Industry. Page 41.

February 6. New England Society of Anesthesiologists. Page 827, issue of November 20.

February 6. American College of Radiology. Page 1001, issue of December 18.

February 9 and 10. Annual Congress on Medical Education and Licensure. Page 786, issue of November 13.

February 23 and 24. American College of Surgeons. Notice above.

March 2–5. New Orleans Graduate Medical Assembly. Page 828, issue of November 20.

March 2–May 4. Massachusetts Department of Mental Health. Postgraduate Seminar in Neurology and Psychiatry. Page 540, issue of October 2.

April 3. New England Society of Anesthesiologists. Page 418, issue of September 11.

April 29 and October 28. New England Obstetrical and Gynecological Society. Page 868, issue of November 27.

May 25–31. First World Congress on Fertility and Sterility. Page 1000, issue of December 18.

District Medical Societies

ESSEX NORTH

January 14. Pentucket Club. 111 Main Street, Haverhill.
May 13. Andover Country Club, Shawsheen.

MIDDLESEX WEST

January 12–March 25. Postgraduate Course in General Medicine.

NORFOLK

January 27.
February 24.
March 24.

Calendar of Boston District for the Week Beginning Thursday, January 8

Thursday, January 8

*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
12:00 m. Consultation Rounds. Cardiovascular. Psychiatry. Boston City Hospital.
*12:00 m.–1:00 p.m. The Surgical Therapy of Pulmonary Tuberculosis. Dr. Norman J. Wilson, Jr. Stearns Auditorium, New England Center Hospital.
5:00 p.m. Case presentation and pathological discussion followed by a subject of special presentation. Joslin Amphitheater, New England Deaconess Hospital.
*5:00–6:00 p.m. Surgical Division Meeting. Mount Auburn Hospital. Cambridge.
8:00 p.m. American Federation for Clinical Research. Children's Medical Center. Jimmy Fund Building, 25 Binney Street.

Friday, January 9

*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit. 57 East Concord Street.
*10:00 a.m.–1:00 p.m. Medical and Surgical Grand Rounds. Dr. George W. Thorn and Dr. Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
10:30–11:15 a.m. Diabetes Lecture. Dr. Elliott Joslin. New England Deaconess Hospital.
11:00 a.m.–12:00 m. Pediatric Conference. Mount Auburn Hospital, Cambridge.
12:00 m.–1:00 p.m. Clinicopathological Conference (Boston Floating Hospital). Joseph H. Pratt Diagnostic Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.
7:30 p.m. Massachusetts Society of Anesthesiologists. Joslin Amphitheater, New England Deaconess Hospital.

Saturday, January 10

*9:00 a.m. Proctology Clinic. Peter Bent Brigham Hospital.
*2:00 a.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*11:00 a.m.–12:00 m. Blood Clinic. Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.
12:00 m. Consultation Rounds Diabetes. (Combined Services). Peabody 3, Conference Room, Boston City Hospital.

Monday, January 12

*8:00–9:00 a.m. Combined Medical and Surgical Rounds for Diabetic Surgery Cases. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by entire Surgical Staff and Anesthesia Staff. Cheever Amphitheater, Dowling Building, Boston City Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*7:00–9:00 p.m. Anesthesia Teaching Conference. Stearns Auditorium, New England Center Hospital.

Tuesday, January 13

*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.
12:00 m. Consultation Rounds. Infectious Diseases. Gastrointestinal. Boston City Hospital.
*12:00 m.–1:00 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.
*12:15–1:15 p.m. X-ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
*5:00–6:00 p.m. Service Meeting followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.
8:00 p.m. Harvard Medical Society. Main Amphitheater, Peter Bent Brigham Hospital.

Wednesday, January 14

*12:00 m. Boston State Hospital Psychiatric Seminar. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Medical Conference. (Children's Medical Center.) Jimmy Fund Building, 25 Binney Street.
12:30 p.m. Weekly Pathological Meeting. Joslin Amphitheater, New England Deaconess Hospital.
*4:00 p.m. Thoracic Conference. Held by Overholt Clinic. Harris Hall, New England Deaconess Hospital.
*4:00–5:00 p.m. Fracture Lecture. Boston City Hospital.
*7:30 p.m. Lahey Clinic Lectures. Coronary Thromboses, Acute and Chronic. Dr. David I. Rutledge. Cardiac Arrhythmias. Dr. Robert E. Foley. Joslin Auditorium, New England Deaconess Hospital.

*Open to the medical profession.